PHYSIOLOGICAL NORMALS

BLOOD CHEMISTRY

(Figures are milligrammes per 100 c.c. unless otherwise stated)

Bicarbonate (alkali reserve)	53 to 77 vols. per cent. CO_2
Calcium (serum)	9·9 to 11·1
Chlorides (as NaCl) :	
Whole blood	450 to 530
Plasma	560 to 620
Cholesterol	170 to 220
Plasma proteins (total)	6·3 to 7·8 gm. per cent.
Plasma albumin	4·5 to 5·2 gm. per cent.
Plasma globulin	1·6 to 2·2 gm. per cent.
Phosphorus (inorganic)	3 to 5
Phosphatase :	
Acid (serum, 1 hour)	under 2·5 units
Alkaline (serum, ½ hour)	3·5 to 13·5 units
Potassium (plasmo-serum)	17 to 22
Sodium (serum)	325 to 350
Sugar (fasting)	80 to 120
Urea	20 to 30
Uric acid	2 to 4
Van den Bergh :	
Bilirubin	0·4 to 1·5 units
Icteric index	1 to 6

BLOOD, NORMAL PHYSICAL CHARACTERS

Bleeding time	2 to 5 minutes
Coagulation time	3 to 4 minutes
Fragility :	
Partial hæmolysis	0·48 to 0·42 per cent.
Complete hæmolysis	0·38 to 0·32 per cent.
Specific gravity	1·052 to 1·064
Sedimentation rate (Westergren)	1 to 8 mm. in 1 hour

HÆMATOLOGICAL NORMALS

Hæmoglobin	85 to 105 per cent. (14 to 16 gm. per 100 c.c.)
Red cells	4·5 to 5·5 millions per c.mm.
Mean red cell diameter	7·2 μ
Reticulocytes	½ to 1 per cent.
Platelets	200,000 to 500,000 per c.mm.

White cells (total)	6,000 to 8,000 per c.mm.
Neutrophils	60 to 70 per cent.
Lymphocytes	20 to 25 per cent.
Monocytes	4 to 8 per cent.
Eosinophils	½ to 3 per cent.
Basophils	0 to 2 per cent.

CEREBROSPINAL FLUID, NORMAL CHARACTERS

Pressure (adult)	150 mm. water
Cells	0 to 5 lymphocytes per c.mm.
Chlorides	700 to 760 mg.
Glucose	70 to 100 mg.
Protein	10 to 35 mg.
Urea	10 to 40 mg.

URINE

Total quantity per 24 hours	1,000 to 1,800 c.c.
Specific gravity	1·010 to 1·025
Reaction	*p*H 4·7 to 8

Average amounts of inorganic and organic solids in 1,000 c.c. of urine from adult on normal mixed diet :—

I. Inorganic constituents :	
Chlorides (as NaCl)	10·0 gm.
Phosphorus (as P_2O_5)	2·0 gm.
Sulphur (as SO_3)	2·0 gm.
Sodium (as Na_2O)	4·0 gm.
Potassium (as K_2O)	2·0 gm.
II. Organic constituents :	
Urea	30·0 gm.
Ammonia	0·6 gm.
Uric acid	0·6 gm.
Creatinine	1·5 gm.
Total nitrogen	14·0 gm.
17-ketosteroids—	
Male	9·9 to 15 mg. per 24 hours
Female	6·4 to 10·2 mg. per 24 hours

FÆCES, NORMAL FAT CONTENT

Total fat up to 25 per cent. by weight of dried fæces :—

Split fat :	
Free fatty acids	9 to 13 per cent. dried fæces
Soaps	10 to 15 per cent. dried fæces
Unsplit (neutral fat)	1 to 2 per cent. dried fæces

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By Various Authors

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NINTH EDITION

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This Book is Dedicated

to

The Right Honourable Viscount Nuffield,

G.B.E., F.R.S., M.A., D.C.L., LL.D.,

in appreciation of his many

Generous Benefactions to Medicine

PREFACE TO THE NINTH EDITION

THE ninth edition appears in a new format, which I trust will commend itself to readers. The general character and scope of the book remains unaltered.

Under present-day conditions in the printing trade a considerably longer period is found to elapse between the setting up of the type and the publication of a book than before the war. Consequently it is impossible and also undesirable to attempt to include details regarding new forms of treatment, such as streptomycin, which are still in an experimental stage. For such the student and practitioner should refer to the current medical literature.

Since the publication of the eighth edition I have to record with great regret the death of Dr. Eric Guttmann, who for many years collaborated with Dr. Desmond Curran in writing the section on Psychological Medicine. Owing to the retirement of Dr. Arthur Maitland-Jones the section on Diseases of Infants has had to be rewritten. I have been fortunate enough to have this undertaken by Professor R. W. B. Ellis.

In view of the increasing employment of the metric system in prescribing, I have added a table of approximate equivalents of weights and liquid measures in the imperial and metric systems. This is placed for quick reference on the inside of the back cover. However desirable the general adoption of the metric system may be in theory, it will probably be many years before it is universally adopted, particularly for the older drugs such as morphia.

While no attempt has been made to increase the subject-matter in the Textbook, the ninth edition incorporates much revised and in some cases rewritten material. Mr. V. E. Lloyd has largely rewritten the sections on Gonococcal Infection and the Treatment of Syphilis and incorporated an ingenious chart for the rapid estimation of dosage in infants with Congenital Syphilis.

In the Chest section Mr. R. C. Brock has rewritten the article on Empyema. Considerable alterations have been made in the section dealing with Diseases of the Thyroid, Addison's Disease, and Diseases of the Pituitary. The articles on Hæmatemesis and Carcinoma of the Stomach have been rewritten. In the Cardiovascular section, apart from minor

revision, the articles dealing with Coronary Sclerosis, Angina and Coronary Occlusion, and Congenital Heart Disease have been rewritten.

Dr. F. M. R. Walshe has rewritten the Ætiology and Pathology of Cerebral Vascular Disease, and most of the sections on Poliomyelitis, Herpes Zoster, the Treatment of Neurosyphilis, Bell's Palsy, and Sciatica. Dr. Desmond Curran has dealt with electrical convulsive therapy and insulin therapy in more detail than in the past, and has also added a section on Psychosomatic Medicine.

In the Tropical Diseases section Group Captain Lipscomb has largely rewritten Malaria, while Dr. Trevor Owen has extensively revised the articles dealing with Diseases of the Liver and the Gall-bladder.

In conclusion I should like to thank reviewers and readers for many helpful suggestions, and my fellow-contributors for their loyal co-operation. I am specially indebted to Mr. D. R. Pugh, Dr. D. R. S. Saunders, and Dr. John Deakin for reading the proofs, and to Mr. D. F. Potter for the revision of the Index. Finally, I wish to acknowledge the unfailing courtesy, patience, and efficiency of the publishers and printers.

J. J. CONYBEARE.

1949.

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INFECTIOUS DISEASES

INTRODUCTION

MANY diseases are caused by a recent or remote invasion or infection of the tissues of the host by a parasite (virus, bacterium, protozoon, metazoon, or fungus). The parasite (causal organism) is potentially transmissible from one host to another; hence, such diseases are *infective*. Among them are some caused by readily transmissible specific parasites, and these are known as the specific, or acute specific, infectious diseases or "fevers"—since "fever," which implies raised *temperature* and quickened *pulse*, is a characteristic symptom.

Modes of Infection.—Infection is commonly conveyed directly from one person to another. Save in the enteric group of diseases, where infection is spread by articles of drink or food, and in certain diseases such as plague, typhus, and malaria transmitted by the medium of infected insects, the usual mode of spread is by spray, droplets, or floating droplet-nuclei projected through short distances by sneezing or coughing. In some diseases, infection may be conveyed by alternative routes, *e.g.*, the virus causal of acute anterior poliomyelitis may be inhaled or ingested. The role played by fomites, *e.g.*, utensils, syringes, bedding, letters, or dust is, in the light of recent research, assuming increasing importance.

Carriers.—A carrier is one who, although not himself suffering from the specific disease, harbours, and is thus in a position to spread, the causal organism. The carrier state may persist for a varying period after a frank clinical attack of the disease which has rendered the patient himself immune. Such persons are termed "convalescent carriers." Persons who have passed through no recognisable clinical attack of the disease can yet carry specific organisms and be immune to the disease; they are "healthy or contact carriers" whose immunity has been acquired by small repeated sub-clinical doses of infection. The carrier state may be transient or permanent. Non-immunes may carry temporarily, *e.g.*, during latent infection or while incubating the disease.

Incubation Period.—Between infection and clinical attack is a latent period termed the incubation period which varies with each disease, and, within certain limits, for the same disease. During incubation the organisms are multiplying and probably in large part being destroyed by the tissues, but ultimately the organisms or their products gain the upper hand, overcome the resistance of the host, and initiate that complex of symptoms and signs by which the "disease" is recognised.

Variations, or apparent variations, in the length of the incubation period of the same disease may depend on any of the following factors: (i) difficulty in fixing accurately the actual date upon which infection took place; (ii) variations in size and virulence of the initial infecting dose and in the existing basal immunity of the host; (iii) an ill-defined onset, particularly characteristic of typhoid fever and whooping-cough.

Table of Incubation Periods

The incubation periods of the commoner infectious diseases fall into three groups—*Short*, *Intermediate*, and *Long*.

I. *Short: within 7 days.*

Diphtheria.

Cerebrospinal Fever.

Hæmolytic streptococcal fevers:

(*a*) Scarlet fever.
(*b*) Erysipelas.
(*c*) Streptococcal puerperal sepsis.

II. *Intermediate: from 7 to 14 days.*

Smallpox: To prodromal stage, 12 days.
To rash, 14 days.

Exanthematic, Louse, or European Typhus, 12 to 14 days.

Enteric Fever: (*a*) Typhoid, 12 to 14 days.
(*b*) Paratyphoid, 10 to 12 days.

Measles: To Koplik's spots, 10 to 11 days.
To rash, 14 days.

Whooping-cough: To catarrhal stage, 7 to 14 days.
To whoop, 14 to 28 days.

III. *Long: from 14 to 21 days.*

Chickenpox, 14 to 21 days.

Rubella, 17 to 21 days.

Mumps, 18 to 21 days.

Infective Hepatitis has an incubation period of from 28 to 30 days, and

Post-inoculation Jaundice of from 50 to 100 days.

Period of Invasion.—The incubation period is terminated by the period of invasion. The onset of this period may be abrupt or insidious. Symptoms and signs of the disease appear, and increase in severity up to a phase of maximum intensity which is known as the *fastigium*. Thereafter the disease processes abate and the period of decline or *defervescence* is entered. This is commonly succeeded by the period of *convalescence* and recovery. It is sometimes the case that the disease, after an atypical or ill-defined invasion period, does not increase in intensity or severity; on the contrary, the symptoms and signs rapidly abate. The attack is then said to have *aborted*. Latent infections or subclinical attacks so mild as to be clinically unrecognisable are far commoner than was formerly believed to be the case. A frank clinical attack of several of the fevers only occurs in a minority of people actually infected.

Lasting active immunity is commonly produced as the result of an attack of an acute specific infection. By the time the stage of convalescence is reached, specific antibodies have been produced by the tissues in considerable amount. They may, however, fail to be produced, at any rate in sufficient quantity, by the time convalescence is reached; in this case the patient may suffer a *relapse* of the disease if reinfection or reabsorption of toxins

should occur. The immunity produced after an attack usually remains at a high level for a number of years ; it wanes with time, and although this is a rare event in the case of most of the common fevers, a *second attack* may occur at a more or less long interval after the first.

Types of Pyrexia.—Rise of temperature is an almost constant manifestation of the acute infections and only fails to occur when the infection is so overwhelming that the tissues are unable to make any effective response. The following types are described :—

1. *Continued.*—The temperature, although showing the usual evening rise and morning fall, never reaches normal during the twenty-four hours.

2. *Intermittent.*—The temperature drops to normal at some time during the twenty-four hours. There is usually an evening rise and a morning fall, but occasionally in children the reverse may occur.

3. *Remittent.*—This term is occasionally employed to indicate a temperature which, although not reaching normal, shows a considerable rise and fall during the twenty-four hours.

4. *Hyperpyrexia.*—This term is employed for temperatures of 106° F. or over.

The onset of pyrexia may be abrupt or gradual. In typhoid fever the rise may be progressive over a number of days—the typical " step-ladder " pattern. Pyrexia may subside gradually over a number of days (*lysis*) or abruptly in the course of a few hours (*crisis*).

Needless to say, pyrexia is a frequent manifestation of disease, apart from the occurrence of the specific infectious fevers ; and, on the other hand, not all attacks of specific fevers are pyrexial.

Certain acute infectious diseases are characterised, at some stage in their course, by a more or less typical rash. The changes produced in mucous membranes as the result of infection are called collectively the *enanthem*, those produced in or upon the skin the *exanthem*. The skin picture to which the term exanthem, rash, or eruption is applied, is made up of certain primary skin lesions or a combination of these lesions. If more than one type be present the rash is said to be dimorphic or polymorphic (pleomorphic).

The following points must be noted in the examination of a rash :—

1. *Distribution.*—The *absolute* and *relative* distribution of a rash are most important points in diagnosis. It is necessary to ascertain not only upon what parts of the body the rash is present or absent, but where it is present most profusely. The site first involved, the abundance and type of the rash, are important.

2. *Type.*—A rash may consist of an *erythema* of any variety, of *macules*, *papules*, *vesicles*, *pustules*, *petechiæ*, or *wheals*, or of any combination of these. The lesions may be *discrete* or *confluent*, either generally or locally.

3. *Colour.*—This is important, especially in considering the erythematous types of rash.

4. *Itching.*—This is an unusual symptom of the acute exanthemata, which, however, sometimes cause intense irritation. The eruptions of secondary syphilis, which must be differentiated from the acute exanthemata, do not itch. The possible effects upon the appearance of the eruption of scratching or treatment—local or general—must be considered.

5. *Prodromal Rashes.*—A prodromal rash is one which appears and, unless petechial, commonly disappears before the rash characteristic of the disease develops. Unless the possibility of a prodromal rash is borne in

mind, a serious mistake in diagnosis may be made. Such rashes are either erythematous (scarlatiniform or macular), urticarial, or petechial, or a combination of these types.

SERUM DISEASE OR SERUM SICKNESS

Following the administration of therapeutic sera, the syndrome known as serum disease may occur due to foreign proteins contained therein. Its frequency and severity have been very much diminished by using " protein-digested " (globulin-modified) products of very low protein content. Serum sickness ordinarily appears between the seventh and fourteenth day after administration. The main features are pyrexia with sometimes a rigor, a rash which is typically urticarial and sometimes pleomorphic, and less commonly, adenitis and arthritis. Transient albuminuria is frequent. The duration of serum disease may be from a few hours to three or more days. The rash, which may be confined to the site of injection, is the most constant phenomenon. Whatever other elements are present, wheals can almost always be found on some portion of the body. The urticarial eruption may be associated with a rash of morbilliform or scarlatiniform type. Serum rashes give rise to intense irritation. This can usually be relieved by an alkaline lotion, but in severe attacks the administration of adrenaline hypodermically (5 to 10 minims of a 1 in 1,000 solution) followed by ephedrine ($\frac{1}{4}$ to $\frac{1}{2}$ gr. three- or four-hourly by mouth) frequently affords rapid relief. In those who are naturally sensitive to protein, signs of serum sickness may appear within a few minutes or hours of administration, and in such patients may be of alarming severity. The symptoms are clinically similar to anaphylaxis. The worst examples occur in those who have never before received serum (*atopics*). Fortunately, only about 1 in 70,000 persons exhibit this extreme serum-sensitiveness or *atopy*. If a period of more than ten days has elapsed between the administration of two doses of serum derived from the same species of animal, the patient may show signs of sensitiveness following upon the injection of the second dose. Hence inquiry should always be made as to any previous administration of serum, and any patient who may be presumed to be serum-sensitive owing to lapse of time since the last injection, or who gives a history of asthma, particularly of horse-asthma, should be *desensitised* before a therapeutic dose is injected.

The method of desensitisation depends upon the route decided upon for the subsequent injection of the therapeutic dose. If this is to be *intravenous*, then 0·1 c.c. of the therapeutic serum (*not* normal horse serum) diluted in 10 c.c. of sterile isotonic saline solution at body temperature is injected *slowly* into a vein. If symptoms of sensitiveness appear following this dose, it is repeated in an hour: if nothing untoward follows the first dose, the second dose may be one of 0·5 c.c. of serum similarly diluted and injected. If intramuscular therapy be proposed, the first desensitising dose consists of 0·1 c.c. of serum diluted 1 in 10, *intradermally*, and a second of 0·5 c.c. similarly diluted, *intramuscularly*. If no signs of serum sensitiveness have appeared after these desensitising doses, the therapeutic dose may be injected one hour later. An urticarial rash, local or general, and, occasionally, vomiting, sweating, respiratory and circulatory embarrassment may follow the injection of the desensitising dose. No therapeutic dose

must be given until, after the last desensitising dose, the patient has shown no signs of sensitiveness, the desensitising doses being continued at intervals if necessary. In all but the slightest cases of anaphylactic manifestations, atropine and adrenaline must be injected at once. Except in intravenous serum therapy, anything save trifling signs of serum sensitiveness are rare, even when the desensitising dose is inadvertently omitted. Nevertheless, desensitisation by the appropriate method must *never* be omitted when there is a past history of serum injection or a personal or family history of asthma, although neither tests for sensitivity nor methods of desensitisation are wholly reliable. Asthmatic patients should *never* receive serum *intravenously*.

E. H. R. Harries.

THE USE OF SULPHONAMIDES

It is most important that the student and practitioner should be thoroughly familiar with the indications which call for sulphonamides and with their toxic effects. The routine administration of such drugs to every patient with fever or evidence of infection, without regard to diagnosis, cannot be too severely condemned. In many diseases, such as influenza, tuberculosis, and enteric fever, sulphonamides are not only useless but potentially harmful. Further, the haphazard administration of sulphonamides in small or irregular doses may render bacteria resistant to the drugs and thereby interfere with effective treatment later. It is clear, therefore, that before prescribing sulphonamides it is essential first to reach at any rate a tentative diagnosis. Even when it has been decided to administer sulphonamides it is almost equally important to select that compound of the group which is best suited to the case.

Mode of Action.—Sulphonamide drugs are bacteriostatic rather than bactericidal, *i.e.*, they inhibit the multiplication of organisms. The fewer the organisms the more effective is the bacteriostatic effect. Moreover, the concentration of the drug in the blood and body fluids must be sufficient to produce bacteriostasis, and hence sulphonamides must be given in the optimum dose to produce and maintain such a concentration for an adequate period, *e.g.*, six to seven days. If clinical response is not evident by that time it will seldom be obtained by prolonging chemotherapy, but the drugs should always be continued for two or three days after apparent improvement to minimise the risk of relapse. Inadequate doses may render bacteria insusceptible to the drug, a condition often described as " sulphonamide-fast." After absorption into the blood stream, part of the sulphonamide is conjugated with acetyl groups, chiefly in the liver. These acetyl derivatives of sulphonamides are excreted in the urine (*vide infra*).

Varieties of Sulphonamide Drugs.—There are numerous trade names for the various sulphonamide compounds, but to avoid confusion the drugs should be prescribed under their recognised non-proprietary names. The term sulphonamide is a general one and does not indicate any particular drug. Those in relatively common use are Sulphanilamide, Sulphapyridine, Sulphathiazole, Sulphadiazine, Sulphamezathine, Sulphamerazine, and Sulphaguanidine. Sulphapyridine should not be used as it has no special advantages and often causes nausea and vomiting.

The following organisms are sulphonamide-sensitive ; the most effective drugs for the treatment of each are given in brackets : *Streptococcus hæmolyticus* (sulphanilamide) ; pneumococcus (sulphathiazole, sulphadiazine, sulphamezathine) ; meningococcus (sulphathiazole, sulphadiazine) ; *Bacillus coli* (sulphamezathine, sulphanilamide) ; gonococcus (sulphathiazole) ; bacillary dysentery (sulphaguanidine).

The following organisms are relatively insensitive to sulphonamide but sensitive to penicillin : *Staphylococcus aureus* ; non-hæmolytic streptococci ; some strains of gonococci. Many diseases such as typhoid, tuberculosis, undulant fever, influenza, and the virus and rickettsial infections do not respond to either sulphonamides or penicillin.

Toxic Effects.—Although these are very uncommon in relation to the enormous numbers of patients taking sulphonamides, they may be very serious ; and every patient receiving sulphonamides should be kept under close medical observation. The toxic effects most commonly encountered are as follows :—

1. *Cyanosis.*—This is practically confined to patients taking sulphanilamide. It is of no pathological significance, though it may make the patient look much more ill than he really is. The colour may be due to methæmoglobin or sulphæmoglobin. *It is never a reason for stopping the drug*, nor is there any object in withholding sulphur-containing foods or medicines, *e.g.*, eggs or sulphates, as was at one time advised.

2. *Nausea and Vomiting.*—These symptoms, including anorexia, are very common with sulphapyridine but not with other sulphonamides. Sulphapyridine should never be used if other equally efficient drugs, such as sulphadiazine or sulphathiazole, are available. If these are badly tolerated, penicillin should be given instead of sulphonamides.

3. *Hæmaturia and Anuria.*—These symptoms are due to blockage of the urinary passages, including the renal tubules, by crystalline deposits of the acetyl derivative of the drug. When the urinary output is small, as in hot climates, the danger is a very real one. The urinary output should be maintained at a minimum of 50 oz. per diem by insisting on the patient taking 5 to 6 pints of fluid daily and by giving sufficient alkalis (sodium bicarbonate and potassium citrate) to keep the urine alkaline to litmus. Warning symptoms are pain in the loins, often radiating towards the groins, hæmaturia, and oliguria. It must, however, be remembered that hæmaturia may occasionally occur as a result of the disease—*e.g.*, cerebrospinal fever—for which the drug is being given. Oliguria and hæmaturia call for immediate cessation of chemotherapy and increased fluid intake. If, however, anuria develops, cystoscopy and passage of ureteric catheters are required and the renal pelves should be irrigated with warm 2·5 per cent. solution of sodium bicarbonate.

Urinary symptoms are most commonly encountered in patients taking sulphapyridine or sulphathiazole, as acetyl derivatives of these drugs are very insoluble in urine, especially if it is acid. There is much less risk in the case of sulphamezathine and sulphamerazine, and none with sulphanilamide.

4. *Sulphonamide Dermatitis.*—This is not an uncommon complication and frequently develops with " drug fever " as a papular erythematous eruption towards the end of treatment. It may be evidence of sensitisation, and if so, the rash will fade rapidly and the patient become desensitised if administration is continued. If evidence of improvement is not apparent

in twenty-four hours the drug should be stopped, as drug retention may also cause a rash and this is liable to be associated with toxic reactions. Sensitised patients may develop an immediate rash if sulphonamide is again administered, even months later, especially if applied locally to the skin.

Patients who are taking sulphathiazole may very occasionally develop a rash resembling erythema nodosum (*vide* p. 62).

In addition there are other toxic effects which may occur occasionally with any of the sulphonamides.

(i) *Leucopenia and Agranulocytosis.*—A mild leucopenia with relative lymphocytosis is frequently observed during sulphonamide administration, but in occasional cases leucopenia may progress to agranulocytosis (*vide* p. 274). The latter is one of the most dangerous toxic effects of sulphonamide treatment, though fortunately rare. It seldom occurs until 30 gm. have been taken. In order to obtain early warning of its imminence a complete white cell count is essential on alternate days in every patient who has taken 25 gm. of the drug. Administration should be stopped immediately if the total leucocyte count falls below 5,000 or the neutrophils below 50 per cent. The symptoms and treatment of agranulocytosis are described on page 274.

(ii) *Drug Fever.*—This occurs chiefly between the fifth and eighth day and is usually low. Recrudescence of infection is likely to occur earlier but may cause confusion. If drug fever is diagnosed the indications for continued administration should be carefully considered, and in any case control with frequent blood counts is essential.

(iii) *Anæmia.*—Various forms of anæmia, aplastic, hæmolytic, or thrombocytopenic, are very rare, but potentially dangerous. The drug should be stopped immediately and the patient transfused with fresh blood.

Methods of Administration.—1. *Oral.*—This is the method of choice. The tablets must be thoroughly crushed, and the powder is best given in milk or water, preferably suspended with a little tragacanth ; the addition of sodium bicarbonate may help to allay gastric irritation. As it is essential to keep up the concentration of the drug in the blood and body fluids the doses must be given at regular intervals, and the *patient should be aroused if necessary*, otherwise the concentration may fall rapidly during the night and bacteriostasis cease.

2. *Intravenous Route.*—This is required when the patient fails to absorb the tablets given by mouth or is suffering from an acute and severe illness, *e.g.*, cerebrospinal fever. The soluble salts of sulphadiazine or sulphathiazole are usually employed. These are given *very slowly* and great care is necessary to avoid the fluid escaping outside the vein. Usually after one or two intravenous injections the patient is well enough to take the drug by mouth.

Dosage in Adults.—This will vary with the severity of the infection. When it is essential to get the patient rapidly under the influence of the drug the initial dose should be large and is often termed the " loading " dose. It is usually 2 gm., *i.e.*, four ½ gm. tablets by mouth or in the more acute illnesses 2 gm. intravenously, but in fulminating infections up to 4 gm. may be given intravenously as a " loading " dose. This is followed by four-hourly doses of 1·5 gm. for the first two or three days. For the next two days the dose is maintained at 1 gm. four-hourly and then for two further days 1 gm. six-hourly. Thus the total during the first two days is

19 gm., during the third and fourth days 12 gm., and during the fifth and sixth days 8 gm., *i.e.*, a total course of approximately 40 gm. It should rarely be necessary to prolong treatment further than six or seven days. A leucocyte count is essential not later than the fourth day, and on alternate days subsequently to detect early any tendency to leucopenia or agranulocytosis.

In less serious and less acute illnesses there is no necessity for a " loading " dose, and for the first two days 1 gm. four-hourly is sufficient. This may be reduced during the third and fourth days to 1 gm. six-hourly and during the fifth and sixth days to 1 gm. eight-hourly.

The dosage of the poorly absorbed sulphonamides (sulphaguanidine, sulphasuccidine) is thrice those given above (*vide* p. 7).

A careful record must be kept of every dose of the drug given. This is best achieved by noting on the temperature chart the amount and the type of sulphonamide used.

Dosage in Children and Infants.—Children and infants, weight for weight, tolerate sulphonamides better than adults. Infants up to six months can be given $\frac{1}{8}$ to $\frac{1}{4}$ gm. four-hourly ; from six months to three years $\frac{1}{4}$ to $\frac{1}{2}$ gm. four-hourly ; from three to five years $\frac{1}{2}$ to $\frac{3}{4}$ gm. four-hourly. In acute illnesses a " loading " dose of double the amount should be given.

PENICILLIN

Penicillin is produced in culture fluids of the mould *Penicillium notatum*. Like the sulphonamides it is bacteriostatic, but, unlike these drugs, it is also to some extent bactericidal. It is effective only against certain organisms, and others are completely insensitive. Unlike sulphonamides it is destroyed in the alimentary tract and therefore has to be given by injection. Intramuscularly it is rapidly absorbed and reaches its maximal level in the blood within five minutes of injection. It is, however, rapidly excreted in the urine, and, unless the dose is very large, the concentration of penicillin in the blood falls to practically nothing in two to three hours. Consequently intramuscular injections are required at strictly three- to four-hourly intervals by day and night.

The organisms which are sensitive and those which are resistant to penicillin are shown in the table below :—

Penicillin-sensitive	*Penicillin-insensitive*
Hæmolytic streptococci.	*B. tuberculosis.*
Non-hæmolytic streptococci (some strains).	*B. coli.*
Pneumococci.	Organisms of Enteric Group.
Staphylococci.	*B. pyocyaneus.*
Gonococci.	*B. proteus.*
Meningococci.	Friedländer's bacillus.
B. welchii and other gas-forming anaerobes.	Dysenteric organisms.
Treponema pallidum.	Vibrio choleræ.
Leptospira icterohæmorrhagica.	Non-hæmolytic streptococci (some strains).
B. anthrax.	Brucella melitensis and abortus.
B. tetanus.	Hæmophilus influenzæ.
B. diphtheria.	Filterable Viruses.
Streptothrix actinomyces.	Protozoa.

From the above it will be noted that penicillin, unlike sulphonamides, has no effect on *B. coli* or dysenteric organisms. On the other hand, it is more effective against cocci, some spirochætes and bacilli of the gas-gangrene

group than are any of the sulphonamide drugs. Although penicillin often has to be used solely on clinical indications, it is important that laboratory facilities should be available in order that the infecting organism may be determined and, if necessary, its sensitivity to penicillin estimated. To give penicillin in infections caused by penicillin-resistant organisms is not only wasteful of time and money, but the repeated injections cause unnecessary hardship to the patient. If no improvement results from treatment with penicillin within three days, it is probable that the organism is a resistant one.

Certain strains of organisms vary in their sensitivity to penicillin. Thus relatively insensitive strains may require much larger doses of penicillin than do the ordinary strains. This is particularly true of the *Streptococcus viridans* and occasional strains of the staphylococcus. In infections which fail to react satisfactorily to treatment, laboratory tests may show an abnormally low sensitivity. In such cases penicillin may be effective if given in doses of two to even ten times the normal amount.

Methods of Administration.—1. *Repeated Intramuscular Injections.*—This is the method employed in general or local infections. The average dose is 20,000 units dissolved in 1 c.c. of sterile water, repeated at three-hourly intervals throughout the twenty-four hours. The injection may be painful, particularly if the penicillin is impure. Pain can be minimised by a slow rate of injection with a fine needle and by using a 1 per cent. sterile solution of procaine as a diluent.

Penicillin is destroyed by heat or by contact with even traces of alcohol or antiseptics. Syringes or needles should therefore be sterilised by boiling or dry heat and must be scrupulously clean.

2. *Intravenous Drip.*—Penicillin dissolved in either normal glucose or saline may be given in an intravenous drip.

3. *Intrathecal Injections.*—This method is indicated in pneumococcal and perhaps other forms of meningitis. Twenty thousand units of the pure penicillin dissolved in 10 c.c. of sterile saline is injected into the theca after running off an equal amount of cerebrospinal fluid. The treatment is repeated at twelve-hourly intervals until the fluid is sterile. In addition, penicillin should be given parenterally and also full doses of sulphonamides to control the primary infection.

Grave dangers may result from accidental infection of the cerebrospinal fluid with non-sensitive strains of organisms which may gain access from contaminated solutions of penicillin. Stringent precautions are required in the preparation of solutions and the technique of administration by this route.

4. *Injection into Serous Cavities.*—Localised collections of pus, *e.g.*, empyema or pyarthrosis, may be aspirated and 50,000 units of penicillin dissolved in 10 c.c. of sterile water introduced every forty-eight hours. As in the case of intrathecal injections, it is essential that this solution of penicillin should be sterile.

5. A relatively slow absorption of penicillin may be effected by intramuscular injection of a penicillin-beeswax-oil suspension. The Injectio Penicillini Oleosa B.P. contains 125,000 units in 1 c.c. The oily injection is viscous and must be warmed to body temperature and well shaken. The syringe should also be warmed. This method of administration is used chiefly in the treatment of gonorrhœa (*vide* p. 114) or in ambulant patients.

6. *Local Treatment with Penicillin.*—Penicillin mixed with sulphathiazole powder may be insufflated over wounds or ulcers. Penicillin cream may be applied to skin lesions, such as burns or ulcers. Lozenges containing 500 units are useful in oral infections.

7. *Penicillin Inhalation* (*vide* pp. 466 and 455).

Toxic Effects of Penicillin.—In striking contrast to sulphonamides, penicillin only rarely produces untoward symptoms. In certain persons, who are apparently sensitive, urticaria, pyrexia, and joint pains may arise up to ten days after the first injection. Benadryl in 50 mg. doses thrice daily is often effective in such cases.

Choice between Penicillin and Sulphonamides.—A decision will often be required as to whether sulphonamides or penicillin should be employed or, indeed, whether the administration of both may be desirable. In making such a decision it must be realised that three-hourly injections throw a much greater strain not only on the patient but on the nursing staff than does the oral administration of sulphonamides. This is particularly true in the case of acute illnesses, such as pneumonia, where the repeated injections are likely to interfere seriously with sleep. From this point of view, therefore, sulphonamides have a great advantage. In diseases, such as gonorrhœa and syphilis, in which the patient remains fit, this objection does not hold good.

There are three absolute indications for the use of penicillin : staphylococcal infections, meningitis of pneumococcal or streptococcal origin, and subacute bacterial endocarditis (*vide* p. 349). Staphylococci are relatively insensitive to sulphonamides, and, in the case of pneumococcal and streptococcal meningitis, penicillin, unlike sulphonamides, can be given intrathecally as well as intramuscularly. In gas gangrene penicillin should be given in conjunction with serum and perhaps sulphonamides. Treatment with penicillin in no way affects the necessity for immediate surgical intervention in these cases.

Penicillin is necessarily the drug of choice against organisms which have become sulphonamide-fast (*vide* p. 6).

Unfortunately many organisms, including some of the most dangerous, are insusceptible to both penicillin and sulphonamides. These include the tubercle bacillus, the typhoid group, the brucella group, cholera, plague, *Bacillus pyocyaneus*, and all viruses. There is, however, reasonable hope that new chemo-therapeutic substances may be developed which will make further inroads on disease.

For infections with *B. coli*, penicillin is quite ineffective, and sulphamezathine should be employed.

Penicillin is of great value as a prophylactic measure in wounds. It is given as early as possible in doses of 20,000 units three-hourly, and continued for three days in the case of flesh wounds and four days in compound fractures. It is also of value as a prophylactic before extraction of teeth or tonsillectomy, and is quite essential when such operations are necessary on patients with valvular heart lesions. If this precaution is not taken there is a very real risk that non-hæmolytic streptococci may produce a bacteriæmia and that some of the liberated organisms may form a focus of infection on a damaged valve.

J. J. Conybeare.

HÆMOLYTIC STREPTOCOCCAL INFECTIONS

(a) *Scarlet Fever.* (b) *Erysipelas*

Many strains of streptococci pathogenic for man, when grown upon blood-agar, hæmolyse the medium, with the result that a wide zone of blanching (β-hæmolysis) appears around each colony. These *hæmolytic streptococci* are divided into *groups* (Lancefield), of which Group A is the most important, and into serological *types* (Griffith). Serological typing of the strain facilitates investigation of a local outbreak of hæmolytic streptococcal infection. Either as primary or secondary invaders, they are the cause of a variety of clinical conditions which are brought about through their properties of *invasiveness* and *toxicity*. These two properties are possessed in varying degree by different serological types, and their relative clinical importance varies with the *site* of infection, the *virulence* of the strain or type (its invasiveness and toxicity), and the *basal immunity* of the host. Certain types which produce a soluble erythrogenic toxin freely are responsible in susceptible (Dick-positive) subjects for scarlet fever, but it is essential to realise that the same type which in one person has given rise to a trivial sore throat may, when transmitted to another under suitable conditions, cause scarlet fever, erysipelas, or puerperal septicæmia.

SCARLET FEVER

Scarlet fever (*Scarlatina*) was first so named by Sydenham in 1676, and his description applied to a form so mild as to consist in his view of a rash and nothing more. He made no mention of a sore throat, but the modern conception of the disease is that it may consist in a sore throat and nothing else.

In England, for a number of years, scarlet fever has been a very mild disease ; its fatality rate is now a fraction of 1 per cent. There is, so far, no evidence of a reversion to the severe forms which occasioned great mortality in this country and elsewhere throughout the eighteenth and the early years of the nineteenth century ; but the disease in Eastern Europe is still severe.

In spite of a high isolation rate for many years, scarlet fever is as prevalent as ever, and this is due to the occurrence of sub-clinical infections, very mild unrecognised cases, and carriers.

Scarlet fever is endemic in countries with temperate climates. The disease may become established in subtropical countries, but in the tropics it is very rarely encountered. Epidemic waves occur at intervals of five to seven years. Very dry years appear to favour great prevalence. " Seasonal incidence is more concentrated on late autumn and winter than formerly, with a reduction in prevalence in the spring and summer months " (H. M. Woods). Scarlet fever is a disease of industrial populations, crowded conditions of life affording opportunities for the spread of infection by close personal contact. It is mainly a disease of childhood. Uncommon in infancy, the incidence rises steadily up to five years of age and then steeply from ages five to ten—the result of school infections. The maximum case

mortality occurs amongst children up to three years of age. At all ages females are attacked in greater numbers than males.

Bacteriology and Pathology.—Scarlet fever is caused by certain strains of hæmolytic streptococci proliferating at the portal of entry, commonly the nasopharynx. Soluble toxins are produced, one of which causes the rash in susceptible (Dick-positive) subjects. Occasionally the causal organism invades tissues damaged by the toxins, producing complications of the septic type.

The *blood picture* shows a polymorphonuclear leucocytosis and eosinophilia.

In the hypertoxic or malignant form of the disease, in which the patient dies in a few hours from overwhelming toxæmia, the only appearances seen post-mortem are general congestion of all organs and hæmorrhages into the suprarenals. Apart from this type of case, death in scarlet fever results from complications due either to toxin damage alone, or to invasion of other tissues by the causal or other organisms. Myocardial degeneration, endocarditis, pericarditis, nephritis, suppurative adenitis, arthritis, and septic broncho-pneumonia are the pathological conditions most likely to be present at autopsy.

Incubation Period.—Two to four days, commonly; extreme limits of one to seven days are recorded.

Classification of Types.—Scarlet fever presents the following clinical types :—

1. *Simple.*—A tonsillitis is followed by manifestations of toxin absorption ranging from trifling to moderate severity.

2. *Toxic.* (*"Malignant"*).—Toxin production and absorption are much greater than in the simple type, and may be overwhelming. The difference in the disease process between 1 and 2 is one of degree only.

3. *Septic.*—Local or general sepsis due to the specific organism *superadded* to toxæmia.

Types 2 and 3 are now of very rare occurrence in Great Britain.

4. *Surgical.*—The infection of *wounds* or *burns*, or the genitalia during the *puerperium*, with the specific organism may result in scarlet fever. The nasopharynx is not infected in these forms which otherwise are indistinguishable clinically from ordinary attacks, and tend to be severe.

Clinical Description.—Typically, an *enanthem* is followed by an *exanthem* or rash, but this may fail to appear or be so faint as to escape recognition. The onset is usually abrupt. Sore throat, nausea or vomiting, headache and shivering, rise of temperature to between 100° and 103° F., and tachycardia *out of proportion to the pyrexia* are the usual symptoms at the onset. The fauces are injected, and, after the first few hours, the tonsils either present a clean, intensely red appearance or are covered with a yellowish exudate which is readily removable. A follicular or lacunar distribution of exudate is not uncommon. Sometimes the exudate is more tenacious, and may have a membranous character which may be mistaken for faucial diphtheria: when removed, however, it is seen to be the slough of an ulcer, and ulceration does not occur in diphtheria. The soft palate is injected and presents, typically, a "stippled" appearance. The *tongue* undergoes the following characteristic changes: (i) "White strawberry" tongue: the dorsum is covered, except at the edges, with a creamy white fur through which the enlarged papillæ project. (ii) "Red strawberry" tongue: the

fur gradually strips from the edges inwards, leaving, after the lapse of three or four days, a perfectly clean, red, congested tongue with enlarged papillæ. Occasionally the tongue assumes a much darker shade of red, and is then known as a " raspberry " tongue. The enanthem is evidence of a hæmolytic streptococcal invasion of the fauces and when present without the rash is termed " septic sore throat."

Twenty-four to thirty-six hours after the initial symptoms the *rash* commences to appear. First to be seen upon the neck, it gradually spreads downwards over the trunk and limbs, but rarely appears on the face. The forehead and cheeks are brightly flushed, with a contrasted area of " circumoral pallor." The rash is a *punctate erythema* : points of deep coloration are set in the centres of irregular small islands of bright red erythema. These are usually so closely set on the trunk as to be confluent, when an appearance of uniform redness with deeper punctations is produced. Commonly a subicteric tinge can be seen. The rash is sometimes blotchy upon the arms and legs. It may often be seen in its typical form upon the inner sides of the thighs, even when it has commenced to fade upon the upper portions of the body. Occasionally the rash produces itching.

Pastia's Sign consists in the appearance of linear brown staining and tiny petechiæ at the flexures, particularly in the elbow and the popliteal space. This sign is present in a large proportion of cases of scarlet fever. Although not pathognomonic, it may yet afford considerable assistance in the diagnosis of a faded scarlet fever rash. The petechiæ are, of course, evident after the erythematous element has faded. The rash fades in the same order as it appeared, and is followed by *desquamation*, of " pin-hole " type, of the affected skin, first visible at the root of the neck and beneath the clavicles about a week after the appearance of the rash ; later, on the trunk, palms (fourteenth day), and soles (twenty-first day).

In the *simple* type of scarlet fever there is frequently some enlargement of the cervical lymphatic glands and a transient albuminuria is not unusual. The temperature falls in three or four days. Convalescence may be interrupted by one or more of the late complications described below.

In the very rare *toxic* type the onset is marked by rigors and hyperpyrexia. Persistent vomiting, diarrhœa, and delirium are common. The rash is characteristically badly formed and dusky in colour. Death may result from the effects of profound toxæmia in from twenty-four to thirty-six hours. Toxic encephalitis is an exceptional component of the syndrome.

The *septic* type, also rare, chiefly seen in children up to three years of age, is characterised by the early occurrence of sinusitis, rhinitis, suppurative cervical adenitis, and sometimes general septicæmia. Broncho-pneumonia is not an uncommon terminal event in these cases.

Complications.—Apart from the septic type of the disease, the complications of scarlet fever manifest themselves chiefly between the second and third week of the illness. They are due to toxic action or to bacterial extension from the portal of entry. The important complications are the following :—

(*a*) *Renal.*—Febrile albuminuria occurring early in the disease is usually of short duration, but occasionally it may persist. Renal complications are to be expected most often during the second or third week. They may follow the mildest initial attack of the disease, and range from albuminuria to acute nephritis with suppression of urine and uræmia. The urine may

contain varying amounts of blood, and in appearance may thus be slightly "smoky" or obviously red.

(*b*) *Cardiac.*—Myocardial inflammation is probably commoner than is generally believed, but slight grades pass undetected. Endocarditis, except in association with secondary rheumatic infections, is not common. Suppurative pericarditis occurs in a very small percentage of cases.

(*c*) *Arthritic.*—Joint pains may occur during the initial toxæmia or during serum sickness. Later in the attack, polyarthritis may be of rheumatic origin. *Streptococcal suppurative* arthritis, *epiphysitis*, and *osteomyelitis* are uncommon but serious complications which must not be confused with rheumatism.

(*d*) *Aural.*—Otitis media occurs in 5 to 8 per cent. of cases. Young children, particularly those who have enlarged adenoids, are most liable to infection of the middle ear by direct spread through the Eustachian tube. Rupture of the drum and the discharge of pus may be quite painless and symptomless, or there may be evidence of acute infection of the mastoid antrum. Rhinitis and adenitis are occasional late complications.

Diagnosis.—Mild cases may give rise to considerable difficulties in diagnosis. With the exception, perhaps, of the true "raspberry" tongue, no *one* sign can be regarded as pathognomonic; *all* the signs and symptoms must be considered. The onset presents nothing characteristic. The occurrence of tachycardia out of proportion to the pyrexia is sometimes of value. The condition of the throat has to be distinguished from various forms of tonsillitis due to other organisms. An absolutely normal condition of the fauces is inconsistent with the early stage of scarlet fever other than "surgical." The appearances may be mistaken for diphtheria, which may also be concurrent. Except in the "surgical" forms, swabbings from the fauces plated on blood-agar overnight yield almost pure cultures showing naked-eye β-hæmolysis of the medium. The thickly furred tongue has to be distinguished from the similarly furred tongue of acute rheumatism. The papillated tongue may be simulated by other conditions, which give rise to an acute or subacute exfoliative glossitis, such as measles or gastro-enteritis in young children. The rash may be confused with that of rubella. Prodromal rashes like those of scarlet fever occur in measles, smallpox, and chickenpox. The irritation produced by a new flannel garment or by inunctions of liniments may give rise to localised rashes of scarlatiniform type. Certain drugs such as belladonna, salicylates, foods, *e.g.*, strawberries, therapeutic animal sera, and enemata may give rise to rashes of scarlatiniform type which may be mistaken for scarlet fever. Circumoral pallor is not peculiar to scarlet fever. Skin diseases such as pityriasis rubra should not be confused if the history, absence of enanthem and pyrexia, and the distribution are considered.

The desquamation of scarlet fever must be distinguished from the "branny" peeling following after measles, and to a lesser extent after rubella. The exfoliation of skin which occurs upon the chest of a child after the application of poultices for some pulmonary condition, and the shedding of layers of dead skin in neglected children, can readily be distinguished. The milder grades of ichthyosis are sometimes confused with the desquamation of scarlet fever; a family history of ichthyosis is frequently forthcoming.

The *Dick test* and the *Schultz-Charlton reaction* may afford some assistance in diagnosis.

(*a*) **The Dick Test.**—As already stated, the specific hæmolytic strepto-

coccus produces a soluble toxin. The latter is employed in an intradermal test with the same technique as the Schick test (*vide* p. 22) to detect persons who are susceptible to the toxin of scarlet fever. A "skin test dose" consists of 0·2 c.c. of a suitable dilution of toxin injected intradermally into the skin of the forearm ; since " pseudo " reactions are rare, a control injection is usually omitted. Readings of the results, which closely resemble those of the Schick test in appearance, are possible in twelve hours. The smallest reaction is to be read as positive. Those who give a positive test are considered to be susceptible to scarlet fever, *i.e.*, including the rash. If the test be negative, immunity to the rash-producing toxin, but not to tonsillitis, may be presumed.

The percentage of susceptibles in the different age groups closely corresponds, in children, to the percentages of Schick-positive reactors. Most persons who have had an attack of scarlet fever at any time give a negative reaction. The reaction is positive in 80 per cent. of cases of scarlet fever during the first three days of the attack ; about the fourth day skin immunity is produced and the reaction is likely to be negative.

(*b*) **The Schultz-Charlton Reaction.**—The reaction of the tissues to scarlet fever toxin is to produce antitoxin. This is present in the blood of the scarlet fever patient for the first time about eight days after the appearance of the rash, and may be detected for many years after the attack. The blood serum of a convalescent injected *intradermally* into a *recent* scarlet fever rash will produce local blanching (the Schultz-Charlton reaction) in from six to eight hours. Usually 0·2 c.c. of a 1 in 10 dilution of scarlet fever antitoxin is injected intradermally : a lower quadrant of the abdomen is a most suitable site owing to the uniform character of the rash in these areas. Although a positive result is pathognomonic, *bright* but *late* rashes or *recent faint* ones may fail to blanch, thus limiting the practical value of the test.

Treatment.—Scarlet fever antitoxin has a profound effect upon the toxæmia of the disease. The dosage ranges from 3,000 U.S.A. units *intramuscularly* for the mild case up to 30,000 units *intravenously* for the severely toxic form. Early administration is all-important. Within twelve hours, temperature and pulse-rate fall, the general symptoms of toxæmia abate or are abolished, and the rash fades ; desquamation is minimal. In toxic cases the effects are dramatic. Antitoxin has no *direct* effect on the invasive (septic) features of the disease, for which sulphonamides or systemic penicillin are indicated.

The patient should be kept in bed until the temperature has been normal for a week ; complications call for a longer period. Milk diet should be given until the temperature has fallen ; fish and minced meat may then be added. There is no advantage in maintaining a milk diet for three weeks, as was formerly advised, with a view to lessening the incidence of nephritis. An early return to a mixed diet does not increase the frequency of this complication, the management of which in no way differs from that required in acute nephritis of other causation. Acute polyarthritis is rheumatic and responds to salicylates. Myringotomy may be required for otitis media. Osteomyelitis of the mastoid and long bones demands prompt surgical measures. In suspected mastoiditis it is wise to withhold the sulphonamides pending expert otological advice, lest the extent of the damage be masked by the drug.

Mode of Spread and Prevention.—Scarlet fever is a disease of relatively low infectivity. Close personal contact is usually necessary for its spread, but recently soiled articles may convey infection. Outbreaks as the result of drinking carrier-infected milk have been recorded, and this possible source of infection must be eliminated. Convalescent and "healthy" carriers are numerous. The convalescent carrier, especially the nasal carrier, may give rise to "return" cases. The specific organisms persist upon the nasopharyngeal mucosa for at least four weeks and isolation should therefore be maintained for this period. Desquamation may be safely ignored, but any breach of mucous membranes, rhinitis, or otorrhœa should be regarded as possibly infective until the causal organism can be shown to be absent. Concurrent disinfection is important. Terminal disinfection should also be carried out.

The Dick test may be performed on contacts. Susceptibles may be *passively* immunised by the injection of 1,500 to 3,000 U.S.A. units of scarlet fever antitoxin. Protection is secured within twenty-four hours and lasts for from ten to fourteen days but no longer.

Active immunisation may be carried out by the injection at weekly intervals of graded numbers of "skin test doses" of scarlet fever toxin. Since reactions may prove to be more severe than an attack of the disease, and the duration of immunity is variable and uncertain, the procedure is only called for under special circumstances.

ERYSIPELAS

Ætiology.—Erysipelas is an inflammation of the skin caused by the entrance of the hæmolytic streptococcus through a breach of surface, such as a minute scratch or a wound. From this focus the organisms spread centrifugally and may ultimately invade a wide area of skin or may penetrate to subcutaneous tissues, producing the urgent surgical condition of *cellulitis*. The organism can be cultivated readily from the spreading margin of the inflammatory process. All ages are liable to attack, but the disease is more serious in infants, the aged, and those debilitated by chronic diseases or intoxications such as alcoholism.

Incubation Period.—From one to seven days are the common limits.

Clinical Description.—In most cases the face is the region affected. Invasion is abrupt and is attended by vomiting, shivering, possibly a rigor, pyrexia, and general malaise. There is a sense of heat and smarting at the affected site, which appears as a patch of dark rose-coloured erythema with a definite raised edge. Sometimes blebs are present. The affected site feels hotter to the touch than the surrounding skin. There is some degree of enlargement and tenderness of the related lymphatic glands. The local condition rapidly extends, and in severe cases the whole of the face may be involved so that the eyes cannot be opened and the features are obliterated. Except at the extremes of age and in the debilitated, who may succumb to septic absorption and terminal pneumonia, the prognosis is good.

Treatment.—The sulphonamide drugs are almost specific and have superseded the older methods of treatment. Sulphadiazine is effective and well tolerated, and to adults is given in doses of 1 gm. four-hourly for the first three days and then reduced to half this amount for a week. The usual

precautions must be observed (*vide* p. 6). Locally, boracic fomentations may be ordered in addition but are not essential. Strict isolation and asepsis are imperative. Penicillin is effective but rarely necessary.

DIPHTHERIA

Ætiology.—Diphtheria is a cosmopolitan but preventable disease which, though endemic in all large centres of population, particularly those of industrial type, exhibits localised epidemic prevalence. Outbreaks in schools and institutions, once of common occurrence, are now increasingly obviated by the immunisation of the susceptibles. The disease is mainly prevalent during the winter months. Incidence falls chiefly upon children up to the age of ten years. The number of cases occurring in children from ages five to ten exceeds those occurring in children under five, a fact obviously correlated with the increased opportunities for infection occurring in those of school age. Diphtheria is uncommon in infants under one year old, but the maximum case fatality occurs in children under five years of age. In children under ten years of age the sexes are fairly equally affected ; above that age females preponderate.

Bacteriology.—The *Corynebacterium diphtheriæ* (Klebs-Löffler bacillus) includes the *gravis*, *intermedius*, and *mitis* strains. The last is the least virulent, being sometimes avirulent, and if so, incapable of causing the disease. The bacillus is found in the false membrane characteristic of the disease, and in the throat and nose of convalescents and of a proportion of healthy people. The organism is a non-motile, gram-positive, non-sporing aerobe which produces a soluble exotoxin possessing special affinity for heart muscle and nervous tissue.

Pathology.—The false membrane varies in appearance and thickness according to its age and situation. It occurs in its most typical form upon the tonsils, the pillars of the fauces, uvula, and soft palate. It occurs also upon the epiglottis, and may extend within the larynx partially occluding the glottis. The trachea and bronchi may be invaded, and the membrane may be detached from these structures in the form of a cast or mould. The membrane itself is the result of a combination of fibrinous exudation from, and necrosis of, the superficial layers of the underlying mucous membrane.

Broncho-pneumonia is a common terminal event in the laryngeal form, either as the result of the direct spread of membrane downwards or of infection by secondary organisms. Although generalised, the effects of toxin upon the muscular and conductive tissues of the heart are most evident. The naked eye changes are those of acute myocarditis. Microscopically, the bundle of His (auriculo-ventricular bundle) may be seen, on occasion, to be virtually disorganised. There are no characteristic naked-eye changes in the nervous tissues.

Incubation Period.—Usually from two to four days.

Clinical Types.—Diphtheria may be classified according to the situation of the membrane. The following are the commonest sites : (i) tonsillar, (ii) pharyngeal, (iii) anterior nasal, (iv) laryngeal. Membrane may also occur upon the conjunctiva, the skin, and wounds ; diphtheria of the middle ear is of uncommon occurrence.

Tonsillar and Pharyngeal Diphtheria.—The onset is frequently insidious, especially in children. There may be nothing to direct attention to the throat until the disease is well established, and this is an important factor in its unnecessarily high mortality. The child appears to be poorly, pale, tired, and dispirited. The temperature is only slightly raised, but the pulse is rapid and of low tension. Vomiting is less common than in scarlet fever. Examination of the throat by the time the practitioner is called usually shows a definite membrane. In tonsillar diphtheria this is generally first visible upon one or both tonsils as a patch of greyish-white colour with well-defined edges. The membrane is definitely growing upon the surface of the tonsil, and surrounding it may be a zone of hyperæmia. It is firmly adherent to the underlying tissue, but can be pulled off and leaves a bleeding surface. In pharyngeal diphtheria, the membrane is more extensive, invading, in addition to the tonsils, other parts of the pharynx.

If treatment is delayed the membrane tends to spread and its colour to become darker owing to the presence of altered blood, and later owing to necrotic changes. There may be characteristic fœtor and œdema of the tonsils and uvula. Some degree of cervical adenitis and periadenitis, except in very mild cases, is usual. In the hypertoxic or " malignant " type of case this may be so pronounced as to give rise to the appearance—always of very grave prognostic import—known as " bull-neck." The rapid spread of *gravis* strain infections, with resulting early and severe toxæmia, must be emphasised—especially as the membrane is at first thin and glairy and thus atypical in appearance. Albuminuria is frequent, but not constant, at the onset of diphtheria.

Anterior Nasal Diphtheria.—Though frequently associated with faucial infection, nasal diphtheria often occurs alone. Owing to its insidious course it may pass unrecognised for perhaps weeks, during which period the affected ambulant child disseminates the disease. Typical nasal diphtheria is characterised by a yellowish blood-stained discharge from one or both nostrils. Examination within the anterior nares may reveal a patch of membrane on the inner or outer walls, or the nares may be occluded by the presence of membrane. Often, however, the membrane may be situated too far back to be seen by ordinary methods of examination. Frequently the skin below the nostrils is excoriated. The child, although not definitely ill, is usually out of condition. A foreign body in the nose may produce a blood-stained nasal discharge which may simulate nasal diphtheria. Occasionally, too, the disease may arise in conjunction with a foreign body.

Laryngeal Diphtheria.—This form, which may be primary but more often is secondary to the faucial form, or, in infants, to a post-nasal focus, is now, fortunately, of very much less frequent occurrence—a result, undoubtedly, of the mass-immunisation of pre-school children (*vide infra*). The symptoms are caused by mechanical obstruction of the glottis by membrane and inflammatory swelling. The condition is most liable to occur in children under five years of age. In infants the onset of obvious laryngeal obstruction may be rapid ; in older children there is usually a phase of noisy breathing with a harsh " croupy " cough. *Inspiratory* stridor occurs. As the condition advances, inspiratory embarrassment becomes urgent ; the accessory muscles of respiration come into play, and there is recession of the lower ribs. Cyanosis, tachycardia, and restlessness are prominent symptoms. Any considerable degree of obstruction renders sleep impossible

and the patient becomes rapidly exhausted. If no relief is afforded, death takes place from asphyxia.

Cutaneous diphtheria must be borne in mind as the possible cause of intractable sores on the face, pinna, scalp or limbs, and associated, sometimes, with pareses and myocardial damage.

Complications.—The complications of diphtheria, with the exception of broncho-pneumonia as an extension in the laryngeal form, and the rare post-diphtheritic hemiplegia, are due to the effects of the toxin upon heart muscle and nervous tissues.

Cardiac Involvement.—Myocardial damage varies greatly in degree but is the commonest cause of death. " Early " cardiac failure may occur as the terminal phase of the initial generalised toxæmia. " Late " cardiac failure may occur at any time after the initial phase has passed, most commonly about the fifteenth day. It is characterised by *vomiting*, subnormal temperature, epigastric pain, an alteration in the character of the first heart sound, and enlargement of the liver. Heart block may occur at any stage and may be transient ; it is especially common and serious in degree in late cardiac failure. Vomiting is a danger signal ; death may follow in a few hours or a few days. In " convalescence " extra-systoles may occur, but in themselves are of no prognostic significance ; as occasional heralds of more serious lesions, they should be regarded with caution.

The following, alone or in any combination, are the commonest varieties of diphtheritic paralysis, the pathogenesis of which is discussed on page 699.

Palatal.—This is usually the earliest as well as the commonest ; the signs are nasal voice, regurgitation of fluids through the nose, loss or limitation of movement, and anæsthesia of the soft palate. The condition is usually bilateral.

Pharyngeal Paralysis.—This is an extension of the palatal paralysis and is indicated by a dysphagia, a characteristic " paralytic " cough, and the escape of saliva from the angles of the mouth.

Ocular.—(*a*) *Extrinsic* : strabismus is common, ptosis rare ; (*b*) *intrinsic* : paralysis of accommodation which is subjective and of short duration is relatively common, but in children, at least, often passes unnoticed, though adults may find themselves unable to read small print. The pupils continue to react to light, and frequently to accommodation also.

Intercostal paralysis is shown by immobility of the costal walls during respiration, associated with increased respiratory excursions of the upper abdomen.

Diaphragmatic paralysis is the most fatal type. There is partial or complete immobility and sagging of the upper abdomen, together with increased respiratory excursions of the costal walls. The mortality from this type of paralysis is very high ; if combined with intercostal paralysis the outlook is virtually hopeless. Paralysis of the diaphragm may be of short duration, and it is occasionally possible, by the continuous administration of oxygen and artificial respiration, to tide the patient over the period of its duration. The use of some type of " breathing machine " has greatly improved the prognosis and has also shown that the condition may endure for as long as two weeks with ultimate recovery. Rarer forms of post-diphtheritic paralysis are adductor and abductor laryngeal paralysis and facial paralysis, usually confined to muscles supplied by the third division of the seventh nerve.

A generalised peripheral neuritis involving most often the arms and legs may occur five weeks or so after the onset of diphtheria. It resembles other forms of peripheral neuritis, and the outlook as regards complete recovery is favourable (*vide* p. 699).

Diagnosis.—Early diagnosis followed by specific treatment is all-important if life is to be saved. The majority of cases of diphtheria can and should be diagnosed upon clinical grounds. Valuable time may be lost if patients with suspected diphtheria be deprived of treatment pending bacteriological confirmation. Bacteriological investigations are important chiefly as an accessory or confirmatory procedure. The bacteriologist can report only upon the presence or absence of diphtheria bacilli ; it is for the physician to make a diagnosis, to be confirmed later by the bacteriologist. It must be realised that the presence of diphtheria bacilli does not necessarily mean that the patient is suffering from diphtheria. In taking a swab care must be exercised to see that it is rubbed firmly over the suspected area. Needless to say, in every case of true diphtheria virulent bacilli are present in the membrane, although not always recovered.

The *differential diagnosis* of tonsillar and pharyngeal diphtheria may be very difficult. Streptococcal tonsillitis may produce a membrane which closely resembles that of diphtheria, but in the former condition there is, as a rule, a more obvious inflammatory condition of the throat, and the membrane is, in fact, the slough of a tonsillar ulcer. The onset of streptococcal tonsillitis tends to be abrupt with pyrexia and flushed cheeks, and there is considerable complaint of soreness of the throat. In contrast is the quiet onset of diphtheria with, at most, slight pyrexia, pallor instead of flush, and little or no complaint of sore throat. Vincent's angina produces ulceration, sometimes disguised by the overlying membrane. Patches of *thrush* in the mouths of infants should readily be distinguished. Its irregular distribution upon any part of the buccal mucous membrane, dead whiteness, easy removal, and the presence of the *monilia albicans* are the characteristic diagnostic points.

As already noted, laryngeal diphtheria is usually secondary to the faucial form, and this fact is an aid to diagnosis ; the condition is practically confined to infants and young children. It must be differentiated from *laryngismus stridulus*, and the wheezing of *bronchial asthma*. Sometimes the severe catarrhal laryngitis occurring at the end of the prodromal stages of measles may produce considerable laryngeal obstruction. Scalding fluids and impacted foreign bodies produce obstruction suddenly ; a history of the accident is usually obtainable. In infants, retropharyngeal abscess is a possible source of error. Among adults such conditions as hysteria, syphilis, or tuberculosis are occasionally misdiagnosed as laryngeal diphtheria. The combination of laryngeal and broncho-pneumonic diphtheria or the pressure of enlarged tracheo-bronchial glands or of neoplasms may give rise to stridor, which is both inspiratory and expiratory.

Treatment.—The essentials of treatment consist in the administration of an adequate dose of antitoxin at the earliest possible moment and absolute rest in bed. The mechanical obstruction which occurs in laryngeal diphtheria may, *in addition*, necessitate relief by intubation or tracheotomy. (The role of penicillin in diphtheria is discussed in connection with carriers (*vide* p. 22).)

Antitoxin was first employed in England in 1895. Its use was attended

by a dramatic fall in the case mortality from the disease, which immediately fell from 30 per cent. or more to 20 per cent. or less, and has continued to show a progressive drop to the present average level of 5 per cent. Other causes have contributed, but the outstanding reason for the decline is, without any doubt, the increased employment of antitoxin in adequate doses.

Protein digested sera (globulins) now in general use contain from 4,000 to 6,000 units of antitoxin per cubic centimetre. Since they are virtually protein-free, serum reactions, even following intravenous injection, are rare—but not therefore negligible (*vide* Serum Disease, p. 4).

Dosage.—Dosage is based upon the extent and apparent age of the membrane and the indications of existing toxæmia. The dose for a child must *never* be smaller than that for an adult. Better results are obtained from a large initial dose than from repeated smaller ones. Too large a dose is hardly possible ; too small a one easily so. Give antitoxin *on suspicion*. Beyond possible sensitisation, no harm can result if the suspicion prove ultimately to be unfounded. Never withhold antitoxin while membrane, however old, is still present. The following approximate scale of initial doses will be found adequate :—

Extent of membrane	(*a*) One Tonsil.			(*b*) Both Tonsils.			(*c*) Both Tonsils with Pharynx or Larynx.		
Age of membrane in hours	24	48	72	24	48	72	24	48	72
Antitoxin in 1,000's of units	8	16	24	16	*32*	*48*	*32*	*48*	*96*

N.B.—Doses underlined should be given wholly or partly by the intravenous route.

For primary nasal diphtheria, 8,000 to 16,000 units, and, for *primary* laryngeal diphtheria, 16,000 to 32,000 units, are usually sufficient, toxæmia being but slight.

Route.—Intramuscular injection into the outer side of the thigh is adequate for cases requiring less than 20,000 units : above this, all or portion of the dose should be injected intravenously. If an additional dose is required it should, if possible, be given intravenously. Oral administration is absolutely useless.

In laryngeal diphtheria, unless the patient be obviously in need of surgical interference when first seen, antitoxin should be given forthwith. A steam kettle is often used. Failure to improve within a reasonable time, increasing stridor, embarrassment of the right heart, and restlessness indicate the necessity for mechanical suction through the direct laryngoscope, intubation, or tracheotomy. The first two procedures are only suitable for hospital practice ; the last is the method to be employed by the practitioner.

Once operation is decided upon, the sooner it is performed the better.

Absolute rest is essential. The patient should remain flat for a week and then be allowed a pillow a week up to three weeks ; then after a week on a couch, walking may be begun cautiously. In toxic cases it is essential to give glucose, 20 gm. in 50 c.c. of normal saline intravenously if possible, and then 4 to 5 oz. diluted in lemonade during each of the first ten days. Careful watch must be kept upon the heart and for signs of paralysis. Palatal

and pharyngeal paralysis may necessitate nasal feeding. Late cardiac failure is to be treated by a return to glucose, intravenously if possible, and the injection of adrenaline. A minute dose of morphia ($\frac{1}{32}$ to $\frac{1}{16}$ gr.) hypodermically is frequently of the utmost value in allaying the fatal restlessness and the distressing vomiting and epigastric pain of myocardial failure. Alcohol and strychnine are of doubtful value in diphtheria. Nikethamide (coramine) is of more use. Digitalis tends to produce heart-block.

The palsies usually clear up spontaneously; massage of the legs and arms is helpful, especially to adults; electrical treatment is seldom required.

Convalescence must not be hurried, and there must be a cautious return to school or occupation.

Mode of Spread and Prevention.—Although there is evidence that mass-immunisation of children (*vide infra*) is decreasing their number, carriers in Great Britain still play an important part in the spread of diphtheria. Carriers, those who harbour virulent strains of the diphtheria bacillus in nose or throat either temporarily or over longer periods, although not at the time suffering from the disease, may be "healthy" or "convalescent." Such "healthy" carriers may be incubating the disease, may be or become immune, but are none the less carriers, who may convey the specific organisms to others, especially in schools and dormitories.

After an attack of the disease the patient remains, for a varying period, a "convalescent" carrier. Most patients undergo spontaneous bacteriological clearance by or before the time they are clinically fit for discharge. The carrier state, which is likely to be maintained by an unhealthy nasopharynx, may yield to fresh air alone, but systemic penicillin in massive doses promises a shorter and more certain cure, and should be tried before resorting to surgery. (*N.B.*—The antibiotic has no effect upon toxæmia and cannot replace antitoxin.) Before release of a patient from isolation it is usual to obtain three consecutive negative swabbings from the nose *and* throat at intervals, preferably of a week. The virulence of the organisms in the chronic carrier state should from time to time be verified. Carriers of avirulent diphtheria bacilli need no segregation.

The *Schick Test* discriminates between those who are susceptible and those who are not susceptible to an attack of clinical diphtheria; it is a test of *antitoxic immunity* not of *infection*. Diluted diphtheria toxin-filtrate is used containing in 0·2 c.c. one-fiftieth part of the minimum lethal dose (M.L.D.) for a guinea-pig. This amount is injected intradermally into one forearm. A precisely similar amount of toxin-filtrate, inactivated by heat, is injected into the other forearm. This acts as a control. If a control is not employed confusion may result because of the occurrence of pseudo-reactions due to sensitiveness to bacterial proteins. These are rare in children under eight years of age, but in older children and adults less rare.

The following readings of the test are possible: (i) *Negative*: nothing is seen on either arm except the needle punctures. (ii) *Positive*: the test arm shows an oval or circular patch of erythema, which later pigments and desquamates the control arm, nothing. (iii) "*Pseudo*" (*negative*): areas of erythema of identical appearance on both forearms disappearing in twenty-four to forty-eight hours. This is equivalent to a negative reaction. (iv) "*Pseudo*" *plus positive*: on both arms an area of erythema appears, but that upon the test arm is larger than that upon the control arm, and presents an inner portion of deeper red; in twenty-four to forty-eight

hours the control arm is clear, and the " pseudo " element has disappeared from the test arm, leaving an ordinary positive test. The " pseudo " plus positive test is the most difficult of the four possible results to read correctly. A positive or " pseudo " plus positive reaction indicates that the person is likely to develop diphtheria if exposed to infection, whereas negative reactors are likely to be immune.

The Schick test possesses a high degree of accuracy. The poorer the circumstances, and the more crowded the environment, the higher is the percentage of negative reactors at all ages. This is due to the greater opportunities for the reception of small immunising doses of the infection.

Immunisation.—The detection of a non-immune should be followed by his protection against the disease. Immunisation may be (i) *passive*, (ii) *active*, or (iii) *combined passive and active*, as recently employed.

(i) *Passive Immunisation* is an emergency measure suitable for immediate contacts. The injection of from 500 to 2,000 units of antitoxin quickly affords protection for a period of two or three weeks.

(ii) *Active Immunisation* is produced slowly, but, with some fall in antitoxic titre, provides lasting protection. It is a regular procedure for the protection of susceptible children, comparable to vaccination against smallpox. The best time to immunise an infant is between six and twelve months of age. The importance of immunisation is greatest in the case of children of pre-school age, but the procedure should also be adopted for all susceptible children of school age, and also for adults, such as hospital nurses who are specially exposed. Since most young children are Schick-positive and therefore susceptible, a preliminary test may be omitted in their case, but for older children and adults it should if possible be done, not only because many are already immune and so do not require artificial immunisation, but because the occurrence of a pseudo + positive reaction is an indication of sensitivity to the prophylactic (*vide infra*).

The prophylactics used in Great Britain are toxoid combined with alum—alum-precipitated toxoid (A.P.T.) and toxoid-antitoxin floccules (T.A.F.). (Toxoid is toxin treated with formalin and thus deprived of its toxic but not of its specific antigenic properties.) Both are potent prophylactics : A.P.T. is usually employed for children under eight among whom it provokes but few reactions ; T.A.F. is reserved for older children and adults, since it rarely gives rise to reactions at any age. For pseudo + positive Schick reactors and those who have reacted strongly to a small preliminary dose of A.P.T., T.A.F. should be used. *At least* two doses of the prophylactic are necessary, and current opinion stresses the importance of a large first dose and a long interval between injections. Suitable doses of A.P.T. are 0·5 c.c. and 0·5 c.c. injected intramuscularly at an interval of at least four weeks ; of T.A.F., three doses of 1 c.c. at intervals of *not less* than two weeks. As a check upon results, Schick tests should be done three months after the last dose. Positive reactors receive a further injection. Reinforcement doses (0·2 c.c. A.P.T.) are of great importance and should be given, as a routine, at or before school entry and at intervals throughout school life. No certificate of *immunity* should be issued unless a recent Schick test is known to be negative.

(iii) *Passive and Active Immunisation.*—Combined active and passive immunisation is advocated for the control of school outbreaks.

MEASLES

Measles (*Morbilli*) occurs all over the world and is endemic in large cities where, in alternate years, it assumes rapid and widespread epidemic prevalence. Commencing in the late autumn, the height of the epidemic is usually attained during the first quarter of the year; by the end of the second quarter the epidemic ceases. Among children under five, and especially under three years of age, concomitant broncho-pneumonia is the cause of many deaths; over the age of five this complication is much less common and much less fatal. Infants under three months of age very rarely contract measles. Since few reach adult life without having suffered an attack, with resulting active immunity, the mother, as a rule, confers placentally transmitted passive immunity upon the infant. This immunity persists for the first three months of life. It then wanes gradually and by the eighth month, or earlier, is at an end. Thereafter, the infant is highly susceptible to measles.

Bacteriology.—The causal agent of measles is a filterable virus. Common concomitant organisms, to which the complications of the disease are mainly due, are hæmolytic streptococci, pneumococci, and the *Hæmophilus influenzæ*.

Pathology.—There are no post-mortem changes characteristic of the disease. The pathological appearances at autopsy are those due to the complications. The chief of these, and the one most likely to kill, is broncho-pneumonia.

Incubation Period.—Ten to eleven days to the appearance of catarrhal symptoms; fourteen days to the rash.

Clinical Description.—The prodromal stage of measles lasts for three or four days. It is a febrile catarrhal period characterised by congestion of mucous membranes and the presence of Koplik's spots. The signs and symptoms of this period are grouped together as the *enanthem*. The period of the enanthem is followed by that of the *exanthem* or rash.

The child at first seems to have a cold with sneezing, and running at the eyes and nose as prominent features; photophobia, epistaxis, and diarrhœa may occur. A few hours after the onset the temperature rises to between 99° and 100° F. Next day the catarrhal conditions persist, and a short, hard cough develops. The temperature continues to rise, with slight remissions up to perhaps 104° F., until the full development of the rash. Only when this begins to fade does the temperature drop, either gradually or with some suddenness.

On examination of the buccal cavity during the prodromal stage, general reddening of the mucous membrane will be noted, with perhaps a blotchy appearance of the soft palate. Most important, *as being pathognomonic of the disease*, is the presence of Koplik's spots.

Koplik's Spots.—These are to be detected in more than 90 per cent. of cases of measles examined in the prodromal stage. They may be present as long as five days before the appearance of the rash, and are thus not only of diagnostic but of prophylactic importance, as their detection permits of the early segregation of the patient with the certainty that he has measles.

Koplik's spots are nearly always bilateral. They appear upon the buccal mucous membrane at the level of the premolar teeth and around the

papilla of Stensen's duct (parotid duct). They must be sought for by gently retracting the angle of the mouth with a spatula and examining in oblique light, preferably daylight. Koplik's spots are made up of a central portion which has been likened to a grain of salt in appearance, set upon an erythematous base. The spots may be few in number, or so closely set as to give the mucous membrane of the affected area the " matt " appearance of ground glass, and are detachable with difficulty. They have usually disappeared by the time that the rash is fully developed.

The Rash.—This first appears at the junction of the hair with the forehead and behind the ears. It spreads in regular order over the face, trunk and limbs, palms of the hands, and soles of the feet. The primary lesion is a macule or maculopapule the size of a lentil or smaller, and of dull reddish colour. The individual macules as they appear soon coalesce

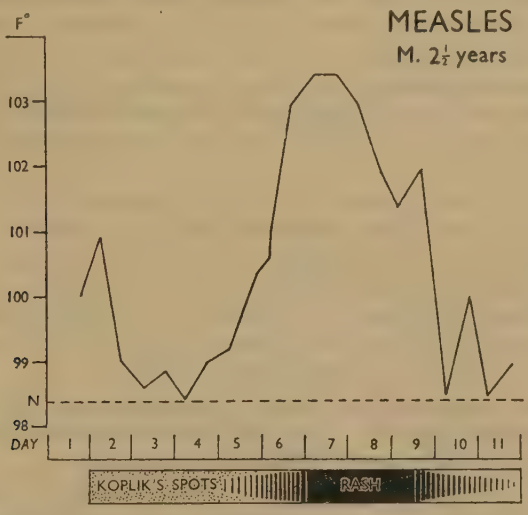

Fig. 1

Temperature chart of an uncomplicated case of measles in child of two and a half years. Exposure to infection was eleven days before onset of symptoms.

into blotchy areas, which frequently present a crescentic margin. The skin is normal between the blotches, but these may become confluent over some portions of the body, giving the appearance of an erythema superficially resembling that of scarlet fever. The rash having attained its full development, which may take twenty-four to thirty-six hours, gradually fades, leaving blotchy staining which is at first purplish and later brown in colour. This staining is usually most marked upon the abdomen. Desquamation of branny type occurs. Prodromal rashes of either scarlatiniform or morbilliform type are not infrequent, and are irregular in distribution and fleeting in character. Measles may be confined to the prodromal stage, the rash never appearing, or the rash may abort. Hæmorrhagic measles is fortunately virtually extinct ; it is invariably fatal.

Complications.—The enanthem of measles affects the mucous membrane of the whole of the respiratory tract. A moderate degree of hoarseness at the height of the stage of enanthem is not unusual, and some degree of bronchitis may be regarded as a normal feature of the disease.

The chief complications of measles are as follows :—

1. *Catarrhal Laryngitis* so severe as to cause recession of the lower ribs may occur towards the end of the prodromal period. The condition, although it may appear alarming, commonly subsides as the rash develops. *Laryngeal diphtheria* as a secondary infection may occur at any stage of measles, and must be differentiated from the catarrhal form.

2. *Broncho-pneumonia* is the chief and most fatal complication of measles, while lobar pneumonia is much less common. Empyema may follow either. Failure of the temperature to fall after the full appearance of the rash should lead to a careful examination of the lungs and the ear-drums.

3. *Enteritis*, due possibly to infection of the bowel by mucopus which has been swallowed, may occur in infants early or late and add to the gravity of the illness.

4. *Ocular Complications.*—The conjunctivitis of the prodromal stage is commonly associated with photophobia. Phlyctenular conjunctivitis and corneal ulcers leaving opacities are not uncommon in debilitated children, as are blepharitis and styes.

5. *Otitis Media*, occurring in the course of measles, is one of the commonest causes of deafness or deaf-mutism in children. Careful watch for *mastoiditis* is essential.

6. *Cancrum Oris* and *Noma* are the terms applied to a rapid gangrenous destruction of the tissues of the cheek and vulva respectively. The infection, which is similar to that causing Vincent's Angina (*vide* p. 445), occurs in neglected, debilitated children. It is now very rarely seen. As in Vincent's Angina, the treatment indicated is systemic penicillin in massive doses.

7. *Encephalitis*, similar to that associated with other acute infections (*vide* p. 632), has occurred in some recent epidemics.

Measles may be associated with whooping-cough or diphtheria, less commonly with scarlet fever. Like whooping-cough, measles may initiate pulmonary fibrosis or light up a latent tuberculous focus.

Diagnosis.—In the catarrhal stage the detection of Koplik's spots clinches the diagnosis. These must not be confused with aphthous patches, or small ulcers of the buccal mucous membrane of dental or gastro-intestinal origin. The severe catarrhal laryngitis which may occur towards the end of the prodromal period is not uncommonly diagnosed as laryngeal diphtheria (*vide* p. 18). The rash of measles has to be distinguished from those of rubella and scarlet fever. The rash of scarlet fever does not occur on the face in punctate form, and the circumoral region is always spared. On the arms and legs, however, it is sometimes coarse and almost blotchy, and may be confused with that of measles. In rubella the colour of the rash is distinctively pink (*vide* p. 28). Occasionally, a *serum rash* may have a morbilliform character, but urticarial wheals are practically always to be seen upon some portion of the body. Certain *drug rashes*, notably that due to the sulphonamides (*vide* p. 6), may be confused. The *tongue* in measles may, on occasion, closely simulate the "strawberry" tongue of scarlet fever.

Treatment.—Bed, an abundance of fresh air, an aperient, and light diet until the temperature has settled are the main requisites. The hygiene of the mouth, nose, and eyes is of great importance. If the cough proves troublesome, some simple sedative mixture is indicated. Complications must be treated as they arise. Sulphonamides or penicillin are indicated

for those due to secondary bacterial infections; these are due chiefly to hæmolytic streptococci.

Mode of Spread.—With the exception of chickenpox and smallpox, measles is the most infective of the "fevers." The maximum degree of infectivity coincides with the prodromal stage. At this stage measles may not only be conveyed by personal contact, but may be spread by droplet-nuclei for short distances through the air, *e.g.*, from bed to bed. The buccal and nasal secretions are highly infective during the catarrhal period, but infectivity rapidly wanes after the appearance of the rash, and by the time that the latter has faded may be considered to have ceased. Articles freshly soiled by secretions in the early stages of the disease may transmit infection.

Prevention.—Unfortunately, the prodromal stage of measles is rarely recognised except in institutional epidemics. When once the rash has appeared and the disease is recognised it is too late by the isolation of the first case to prevent others.

Since measles is very much less fatal to children over five years of age, any method which will postpone the almost inevitable attack until infancy has passed will result in the saving of many lives. The virus, grown on chick embryos, has been used for active immunisation upon a small scale

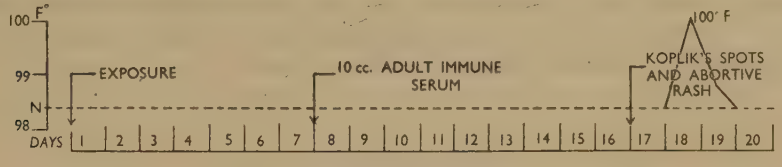

FIG. 2

Diagram of measles attenuated by injection of adult-immune serum. Note prolonged incubation period and attack of trifling severity, resulting in active immunity.

with a measure of success. Injections of the *pooled* serum of convalescents or of adults who have had measles, *parental whole blood*, and, more recently, *gamma globulin*, are successfully employed for either of two *prophylactic* measures—(i) *Sero-prevention*: injected within the *first five days* after exposure, human serum, by conferring temporary passive immunity, prevents the attack in a high percentage of those exposed and injected; (ii) *sero-attenuation*: serum injected within the first five days of exposure in half the dose used for prevention modifies the expected attack. Unless too highly modified, permanent active immunity results from this modified attack.

Donors must be shown to be free from syphilis, and their serum must be pooled and tested for sterility by the bacteriologist. Batches of pooled serum, especially adult serum, vary widely in protective value. The donors must be young; serum derived from the elderly may have little value. In any case, and especially for prevention, adult serum is inferior to recent convalescent serum and should be injected in at least double the dose. *Gamma globulin*, the third fraction into which serum globulins have been separated by Cohn and his co-workers, is believed to contain the chief immune bodies occurring in human blood. It is highly concentrated, and the results of field observation indicate its great superiority over the older

preparations. These it will undoubtedly replace when sufficient supplies are available. For healthy children, attenuation is to be preferred; for others, prevention. The following scale of doses is suggested for children under three years of age :—

Dose under Three Years	*First to Fifth Day after Exposure*	
Serum	*Prevention*	*Attenuation*
Convalescent serum . .	5 c.c.	2·5 c.c.
Adult serum . . .	10 c.c.	5·0 c.c.
Parental blood . . .	...	10 to 15 c.c.

Parental whole blood may be withdrawn from either parent who may be immune, and injected intramuscularly at once. The dose for *attenuation* in children under three is from 10 to 15 c.c. injected into the buttocks.

The disease is in its most highly infective period during the whole of the catarrhal period, and isolation commenced only when this period has passed is of greatly diminished value. A period of isolation of *nine* days, from four days *before* to five days *after* the appearance of the rash is sufficient. Exposed susceptible children should be kept under observation for fourteen days, or seventeen days if serum-prophylaxis has been employed, since attenuation may lengthen the incubation period.

GERMAN MEASLES

German measles (*Rubella*) is usually a disease of trifling severity and world-wide distribution. In Great Britain it occurs in epidemic form in the spring and early summer. It affects children above the age of infancy and young adults. The causal organism is believed to be a virus. The disease is much less infective than measles.

Incubation Period.—From fourteen to nineteen days, occasionally twenty-one days. Common periods are seventeen or eighteen days.

Clinical Description.—In children there may be no appreciable prodromal period, the appearance of the rash being the first indication of anything abnormal. Adults, however, may complain of headache, slightly sore throat, general malaise, and stiffness of the neck for twenty-four hours or so before the appearance of the rash. The prodromal period, if present, is always of short duration. Slight conjunctival injection may occur, and occasionally slight coryza and cough. Koplik's spots are never present. There may be a moderate rise of temperature to 101° to 102° F., which may persist for two or three days. An increase of Türck and plasma cells in the blood occurs.

The rash, which sometimes produces itching, consists of *pink* macules ranging in size from a pin's head to a lentil and occasionally palpable to the finger, appears first, as a rule, upon the face, including the circumoral area, next upon the trunk, and last upon the limbs. This order is not invariable; it may be reversed. It is common for the rash to fade from the site at which it first appeared before erupting elsewhere. The macules may remain discrete

or they may coalesce into blotches which lack the crescentic margins seen in measles. They may remain discrete in one area and become confluent or scarlatiniform in others. The rash is usually most typical upon the abductor aspect of the thigh and upon the dorsum of the foot. The colour of the rash, whatever its type and distribution, is neither the dull red of measles nor the bright red of scarlet fever, but definitely pink. By the second or third day after its appearance the rash fades. If it has been intense, faint yellowish discolorations, quite different from the staining left by the measles rash, may be noted; these soon disappear. There may be scanty desquamation of "branny" type. Palpable enlargement of the posterior cervical and sub-occipital glands and sometimes of the axillary, epitrochlear, and inguinal groups is characteristic. Neuralgic and "rheumatic" pains and mild encephalitis have occurred as complications. Deaths ascribed to rubella are probably due to some concurrent condition.

Recently attention has been drawn, particularly by Gregg, Swan, and other Australian observers, to *congenital defects*, *e.g.*, cataract, deafness and morbus cordis, occurring in infants whose mothers were attacked by rubella during the early months of pregnancy. The sequence is under further investigation.

Diagnosis.—The diseases with which rubella is most likely to be confused are measles, scarlet fever, the roseolar rash of secondary syphilis, and glandular fever (infective mononucleosis).

(*a*) *Measles.*—The definite prodromal period of three to four days, the well-marked coryza, conjunctivitis, and the appearance of Koplik's spots during this stage should serve to prevent confusion with rubella. The rash of measles is dull red in colour, as compared with the pink of rubella.

(*b*) *Scarlet Fever.*—The scarlatiniform phase of rubella is frequently mistaken for mild scarlet fever. Points in favour of the latter are a sudden onset with sore throat and vomiting, tachycardia out of proportion to the pyrexia, and the appearance, twenty-four to thirty-six hours after onset, of the typical rash commencing at the neck and spreading in regular fashion downwards. If in doubt, the Schultz-Charlton reaction may be performed (*vide* p. 15), and swabbings from the fauces plated on blood-agar (*vide* p. 14).

(*c*) *Secondary Syphilis.*—The history, other signs of secondary syphilis such as snail-track ulcers on the fauces, alopecia, anæmia, and the Wassermann reaction should prevent this very serious mistake. The rash of rubella appears first on the face, while in secondary syphilis the face escapes. The rash of rubella is sometimes irritating; the eruptions of secondary syphilis, on the other hand, do not itch. Both conditions are associated with enlargement of groups of lymphatic glands.

(*d*) *Glandular Fever* occasionally shows a roseolar rash which may be mistaken for that of German measles. In glandular fever the blood picture, glands, and the Paul-Bunnell test usually make the diagnosis certain.

Treatment.—Bed, an aperient, and light diet for a few days constitute the only treatment necessary.

Prevention.—Rubella, owing to its long incubation period and indefinite onset, may give rise to administrative difficulties in institutional outbreaks. Infectivity is of short duration. Isolation is only necessary until the rash has faded; five days are ample, as a rule. Concurrent disinfection of everything soiled by the patient is essential.

WHOOPING-COUGH

Whooping-cough (*Pertussis*) is now the most serious of the endemic specific infections of children living in large towns. This is due to (i) the high incidence among infants, although no age is exempt ; (ii) the duration and debilitating character of the illness ; (iii) the liability, at any stage, to concomitant broncho-pneumonia ; and (iv) the danger of permanent damage to the lungs. The disease is most prevalent in the early spring, when broncho-pneumonia is also rife ; it tends to attain epidemicity every other year, sometimes concurrently with measles. The *Hæmophilus pertussis* of Bordet-Gengou occurs in abundance in the droplet spray expelled in the early stages of the attack, but is less easily recovered as the disease progresses.

Incubation Period.—Seven to fourteen days to the catarrhal stage. The paroxysmal stage commences from seven to fourteen days later.

Clinical Description.—Typically, the disease presents two stages : (i) *a febrile catarrhal stage* characterised mainly by pharyngitis and tracheitis due to the multiplication of the specific and associated organisms. After a week or ten days this stage merges into (ii) *an afebrile stage* of paroxysmal cough produced by the sensitisation of respiratory mucosa by a specific endoneurotoxin absorbed during the catarrhal stage. The catarrhal stage resembles a persistent common cold upon which is superimposed a harsh cough. The coughs are at first single, but soon become " grouped," and at length paroxysmal. The first paroxysm terminated by a " whoop " is usually heard at night. Vomiting after coughing is very suggestive of whooping-cough before the whoop appears.

During an uncomplicated attack the paucity of pulmonary physical signs is throughout strikingly disproportionate to the severity of the cough. In infants and the aged the illness may be confined to the catarrhal stage, or no typical whoop may occur. In infants paroxysmal sneezing may precede, follow, or replace entirely the paroxysmal cough.

The *paroxysm* may be divided into three stages : (i) a short inspiration (not constant) ; (ii) a series of short sharp coughs which appear to gather speed and violence ; and, finally, (iii) a long-drawn inspiration ; the sudden entry of air into the emptied lungs through a partially closed glottis gives rise to the characteristic whoop. The paroxysm is frequently succeeded by the vomiting of mucus and food particles. The number of paroxysms, which are always more frequent at night, may vary from as many as fifty to as few as two or three in the twenty-four hours ; their frequency and completeness are indications of the severity and progress of the case. Although many weeks may elapse before they cease entirely, the paroxysms gradually become incomplete, atypical, and occasional. Some children retain the " habit " of whooping long after they have ceased to be either ill or infectious.

A paroxysm may come on quite suddenly. Emotional excitement, change of posture, and particularly the swallowing of food, may suffice to bring on an attack. During the paroxysm which, once started, nothing avails to stop, there is intense venous congestion of the face, which assumes an almost bloated appearance, with conjunctival suffusion and sometimes epistaxis. When the paroxysm ends, the child rapidly recovers its ordinary appearance and its equanimity.

During the expiratory coughs the tongue is projected violently and repeatedly over the lower central incisor teeth. In this way the frænulum linguæ at length becomes abraded, and in some cases an ulcer is produced.

Besides epistaxis, *subconjunctival hæmorrhages* are frequent. Less common is bleeding from the *membrana tympani*. Hæmoptysis and hæmatemesis have been recorded.

Complications.—The complications of whooping-cough are more serious and dangerous than the disease itself. They are as follows :—

Respiratory.—Broncho-pneumonia is common, and frequently fatal in young children ; lobar pneumonia is much less common. Empyema occasionally follows either. Emphysema of any type may occur.

Nervous.—Convulsions may occur in infants and young children. The attack usually succeeds a paroxysm. Cerebral hæmorrhage may prove rapidly fatal.

Otitis Media, as the result of secondary infection of the nasopharynx, may occur, as in measles and scarlet fever.

Hernia and Prolapse.—In the infant the violence of the paroxysms may give rise to hernia. Increase in the size of an existing umbilical hernia is common. Prolapse of the rectum may occur and be difficult to control.

By far the commonest and most important complications are broncho-pneumonia and convulsions.

Whooping-cough and measles not uncommonly occur together. Diphtheria, as a secondary infection supervening at any stage, naturally increases the gravity of the prognosis.

Sequelæ.—Some degree of emphysema may persist. More important is the occurrence of fibrosis and bronchiectasis after broncho-pneumonia or the possibility of activation of a latent focus of tuberculosis.

Diagnosis.—Clinical diagnosis in the catarrhal stage may be impossible. A continued harsh cough which increases in frequency and severity from day to day, without adequate physical signs to account for it, is suggestive, particularly if followed by vomiting. The following accessory procedures may afford assistance : (i) *Cough-plates*—Petri-dishes containing a defibrinated, preferably human, blood medium are exposed 4 or 5 in. from the child's mouth in order to collect spray (not sputum) during the act of coughing. After incubation for three days the pearl-like colonies of *H. pertussis* may be discerned. (ii) *Post-nasal swabs* inoculated upon plates of the same medium, treated with a few drops of penicillin, give equally good results, and in infants are to be preferred to cough-plates. The swab wire is bent to a suitable angle in order that it may be passed behind the uvula. (iii) *Blood-count*—During the early paroxysmal stage there is a high *lymphocytosis*. (iv) The blood *sedimentation-rate* is often *retarded* ; in other infections the rate is *accelerated*. Acceleration of a previously normal or retarded rate gives early warning of secondary infection.

Gold and Bell suggest that a diagnostic triad of suspicious cough, lymphocytosis, and a retarded sedimentation-rate is peculiar to whooping-cough. Specific *complement-fixation* and *agglutination* may be demonstrated in a high proportion of cases, but only late in the disease. *Skin tests* for specific allergy are as yet unreliable, but are being improved.

Before the cough becomes definitely paroxysmal it may be confused with ordinary bronchitis. When the whoop is definitely established there can hardly be room for doubt.

Treatment.—The taking of food or drink may start a paroxysm followed by vomiting, and thus the child may become under-nourished. Food must be given slowly in small quantities at a time. If vomiting is troublesome it may be necessary to feed the patient immediately *after* a paroxysm, as food is then usually retained.

The treatment of whooping-cough is unsatisfactory. If injected in the *earliest* stages of catarrh, vaccines *may* mitigate the duration and severity of the attack, but this cannot be counted upon; injected only in the paroxysmal stage, they are useless. Some have claimed a measure of success for convalescent serum, however, only if given very early.

Drugs.—Linctus scillæ Co. (B.P.C.) in $\frac{1}{2}$ to 1 drachm doses is useful in the catarrhal stage. For the control of the paroxysms, *Tinct. belladonnæ* increased daily to the limit of tolerance is sometimes of value in mild cases; for those more severe, *ephedrine* ($\frac{1}{12}$ gr. for an infant to $\frac{1}{2}$ gr. for a child of five) may be combined with belladonna; for very severe paroxysms, *phenobarbitone sodium* ($\frac{1}{24}$ gr., infants; $\frac{1}{6}$ gr., under five; and $\frac{1}{3}$ gr., over five) is frequently effective. The drug must be withdrawn as soon as possible. For broncho-pneumonia the sulphonamides are invaluable. The *H. pertussis* is insensitive to penicillin, but the concomitant organisms are controlled by its use if the sulphonamides are contra-indicated. These agents, especially in conjunction with oxygen tents, have saved the lives of many infants suffering from this dangerous complication.

Mode of Spread.—Whooping-cough is spread by infective droplets or spray, especially during the catarrhal stage. Recently soiled articles of personal use are also capable of transmitting infection. Whooping-cough must be considered as infective until *one month after the commencement of the whoop*; the causal organism is then rarely recoverable on blood-plates or from post-nasal swabbings.

Prevention.—Prophylaxis is of the utmost importance. Segregation, to be effective, must be early and include those who are merely suspect. Vaccines prepared from *H. pertussis* in the correct antigenic phase possess some prophylactic value, but, so far, type and dosage are not agreed and results vary widely. The *concurrent* disinfection or destruction of articles of any sort used or soiled by the patient is of infinitely greater importance than the *terminal* disinfection of room or bedding.

MUMPS

Mumps (*Epidemic Parotitis*) is endemic in all large centres of population, and is most prevalent during the winter and early spring. Children of school age and adolescents are most susceptible to the disease, and institutional outbreaks are common. The causal agent is a filterable virus with neurotropic affinities and is present in the saliva and nasal discharges during the early days of the attack.

Incubation Period.—Seventeen or eighteen days are common periods, occasionally twenty-one days.

Clinical Description.—There may be no prodromal symptoms. In young adults and some children, general malaise, shivering, rise of temperature to about 101° F., epistaxis, and complaint of stiffness of the muscles of the neck may initiate the prodromal stage. Sore throat is not uncommon.

The prodromal stage may continue for three days, or exceptionally longer, before localising signs are apparent. Swelling of the parotid is first detected in that portion which lies between the posterior margin of the ramus of the mandible and the mastoid process. At first quite slight, and only appreciable to palpation, it rapidly increases. The resulting tension of the overlying tissues results in a characteristic uplifting of the lobe of the ear. Confirmation of the diagnosis of mumps may be afforded at an early stage by the appearance of papillitis at the orifice of Stensen's duct (parotid duct), by tenderness on pressure upwards and backwards behind the angle of the jaw, and by the occurrence of a lymphocytosis.

By the third or fourth day from the commencement of the process the whole of the gland, including the portion overlying the masseter, has reached the maximum degree of enlargement. Adjacent tissues become œdematous ; the skin is stretched and may be slightly reddened. The disease may remain unilateral, but usually both glands are affected, successively or simultaneously. When the swelling is at its greatest, the patient experiences difficulty and pain upon attempting to open his mouth. Saliva, which at first dribbled from the corners of the mouth, becomes scanty, the mouth dry, and the tongue furred. The temperature may remain high for a week. The submaxillary and sublingual glands may be involved. During epidemics, cases have been detected where the process has been confined to one or other of these glands, the parotids escaping. Associated enlargement of neighbouring lymphatic glands is usually present. Albuminuria is frequent ; deafness is a common complaint during the height of the swelling. The enlargement gradually subsides, and in about a week or ten days the parotids have returned to their normal size. Suppuration *never* occurs unless secondary infection has taken place.

Central Nervous System.—The illness may commence, especially in adults, with meningeal symptoms. In the meningeal reaction of mumps clinical signs of meningitis are not conclusive or complete. The cerebrospinal fluid is under pressure, but quite clear ; there is an excess of lymphocytes ; the fluid is sterile on culture ; it reduces Fehling's solution. Meningo-encephalitis may occur at any stage ; it is sometimes concomitant with orchitis. The optic, facial, and auditory nerves may be involved. Occasionally optic atrophy and permanent nerve-deafness result. The most prominent symptoms are usually headache and vomiting.

Orchitis.—Mumps is peculiar in that metastatic involvement of other glands, notably the testes, may occur. In some epidemics orchitis is much commoner than in others. It usually occurs about a week or ten days after the initial parotid swelling, and as a rule one testicle only is affected. Exceptionally orchitis occurs simultaneously with the parotitis, and rarely it may be the first or even the only manifestation of the disease. Orchitis is rare before puberty, but common in adolescents and young men. Testicular pain and tenderness are very severe and constitutional disturbance considerable. Both the body and the epididymis may be affected, and atrophy may result. In girls mastitis and rarely oöphoritis may occur. Acute pancreatitis occurring a few days after the initial parotid swelling, or much later in convalescence, is an uncommon but well-recognised complication, especially in children.

Diagnosis.—In the presence of an epidemic of mumps the diagnosis can hardly be in doubt. The appearance of a fully developed case is

unmistakable. Parotitis occasionally occurs in the course of other infections, especially typhoid, and is usually suppurative. In Mikulicz's disease (*vide* p. 295) there is chronic symmetrical enlargement of all the salivary and also of the lachrymal glands. Salivary calculus and tumours of the parotid may be easily excluded. An inexcusable error, which may be attended by disastrous results, is to confuse the " bull neck " of hypertoxic diphtheria (*vide* p. 18) with mumps. One glance at the throat would serve to prevent such a disaster. The converse mistake is also made.

Treatment.—Bed in a well-aired room, an aperient, and a light diet in a form which can easily be swallowed are commonly all that are necessary. The hygiene of the mouth is important. For orchitis, a suspensory bandage and applications of some soothing preparation such as glycerin of belladonna may be used.

Mode of Spread and Prevention.—Mumps is conveyed by droplet infection ; the disease is not highly infective. It is probable that infectivity ceases concurrently with the subsidence of swelling, but the usual practice is to maintain isolation for a week after the last gland to be affected has returned to normal, an average period of two weeks from onset. Non-immune contacts should be kept under observation (*not* in quarantine) for at least three weeks from the date of the last known exposure. Concurrent disinfection of soiled handkerchiefs and utensils is important.

SMALLPOX

Smallpox (*Variola*) occurs under all climatic conditions. The disease is endemic in India and in parts of Northern Africa. The West Indies and South Africa are among the endemic foci of a milder type of the disease. Smallpox occurs in epidemic and, in the past, has occurred in pandemic form. The last pandemic, in 1871-72, caused 40,000 deaths in the British Isles. In 1901-04 an epidemic resulted in some 4,000 deaths in England and Wales. Since that time the mortality from the disease has steadily fallen in this country owing to a change in the clinical type. The disease shows seasonal prevalence. In countries of temperate climate it is a " cold weather " disease ; fewest cases occur in the summer. L. Rogers holds that the prevalence of smallpox in endemic centres is dependent upon the absolute humidity of the atmosphere. Low absolute humidity favours, while high checks the prevalence of the disease.

The causal agent is a filterable virus and occurs as the elementary bodies of Paschen in the vesicle fluid. Guarnieri's inclusion bodies are aggregations of these. The virus is identical with that of vaccinia (*vide* p. 39). Strains of the same virus of differing virulence give rise to clinical types of smallpox varying in severity. " The viruses of vaccinia, alastrim (*vide infra*), and of a severe case of confluent smallpox all alike act specifically to anti-vaccinia serum, both in the complement-fixation and in the agglutination test " (Mervyn Gordon). There are two chief strains of the virus : (i) Eastern, causing smallpox of the " classical " type (*variola major*) ; (ii) Western, derived from the United States or from the West Indies, causing cases of a mild or relatively mild type (*variola minor* or " alastrim "). This form occurred in England and Wales in 1922. After several years of prevalence, *variola minor* died out in the British Isles. During the recent war, *variola*

major was introduced at British ports from time to time : the only resultant outbreak of any magnitude occurred in Scotland in 1942, and this was controlled by mass vaccination. In the winter and spring of 1946-47 the disease was introduced at ports on several occasions, but its spread was similarly controlled.

The case fatality rate of *variola major* varies in different epidemics ; it may range from 15 to 30 per cent., whereas the fatality rate of *variola minor* is a fraction of 1 per cent.

Pathology.—Apart from the cutaneous lesions, nothing characteristic is to be seen at autopsy. Myocardial degeneration is marked as it is in death from other toxic processes. The spleen is enlarged and soft. Signs of fatty degeneration may be present in the liver and kidneys. The lungs frequently show evidence of broncho-pneumonia.

Incubation Period.—This is very constant in *variola major* : twelve days to the onset of the prodromal stage, fourteen days to the first appearance of the eruption.

Clinical Description.—(*a*) *Variola major.* The *prodromal stage* of smallpox lasts for two or sometimes three days. The onset is usually, but not always, abrupt. Headache, vomiting, severe pain in the back and limbs, shivering and pyrexia are common prodromata. The temperature steadily rises and may reach 104° to 105° F. by the second or third day. Delirium is not unusual. Relaxation of muscular tone occurs, particularly well seen in a characteristic fatigued expression of the face. *Prodromal rashes* sometimes appear and may be petechial, erythematous, or urticarial. The petechial type, always indicative of a severe attack, invariably appears in the flexures of the groins, extending upwards as far as the umbilicus and downwards to some two inches below Poupart's ligament. The rash is most dense over this area, although it may extend up the flanks towards the axillæ. Being petechial, it persists for some days after the appearance of the eruption proper. The other prodromal rashes appear earlier than the petechial forms. Although characteristically patchy and fleeting, these rashes usually invade the " bathing drawers " area, and may persist until the eruption of papules, and then fade. The blood picture shows a leucocytosis with mononucleosis and neutropenia. During the pustular stage neutrophilia develops.

Stage of Eruption.—1. *Papular Stage.*—The eruption commences to appear as a rule upon the third day. It takes two, three, or sometimes four days to complete its evolution. The lesions are at first tiny macules, which soon become papules, set deep in the skin and surrounded by an areola. The focal lesions of smallpox appear in a definite manner, which it is of the highest importance to observe in order that a correct diagnosis may become reasonably certain. Not only do the lesions appear in a definite order, but they attain a definite distribution and relative density following certain well-defined laws which were worked out by Ricketts.

In point of *time* of appearance the lesions appear in the skin in the following order : forehead, face, and scalp ; wrists and the backs of the hands ; trunk, chest, back, and abdomen ; legs and feet. They may also appear in the buccal cavity, especially on the soft palate, on the tracheobronchial mucous membranes, including the larynx, and occasionally upon the conjunctiva.

In point of *density* the following distribution is observed. In the first

place, the lesions of smallpox tend to occur profusely upon any sites which have been irritated during the period of incubation or which have been subjected to pressure; they appear most profusely upon exposed parts and upon convexities. In the fully erupted papular stage the lesions are distributed centrifugally in the following order of *decreasing* density: the face; the wrists and backs of the hands; the forearms; the back; the feet and the extensor aspects generally. The lesions occur much more sparsely upon areas of the skin which are normally protected, such as the chest and abdomen, the inner aspects of the thigh, the groins and the axillæ. So regularly is the axilla free or relatively free from the eruption in smallpox that Ricketts termed the phenomenon "the sign of the axilla."

When the eruption of papules is complete, the temperature usually falls and the patient expresses himself as feeling much better. The rise of temperature in the prodromal stage is due to toxæmia which does not always entirely disappear with the completion of the papular stage, but commonly does so.

2. *Vesicular Stage.*—Gradually the papules become converted into vesicles; associated with this change is an increase in the area and brightness of the areola which surrounds each lesion. The vesiculation of the papules is completed in two days as a rule. The apex of some of the vesicles may show "umbilication." If the wall of a vesicle be punctured with a needle it does not collapse, owing to the multilocular character of the vesicle. For some twenty-four hours the contents of the vesicles remain clear; they then become opalescent. This is the beginning of the pustular stage.

3. *Pustular Stage.*—With the commencement of pustulation, the temperature, which has remained low since the completion of the eruption of papules, again begins to rise, and continues to do so until the stage of pustulation is complete. This secondary rise is due to septic absorption. The stage of pustulation takes four or five days to complete. The lesions swell up and assume a tense hemispherical appearance; the areola fades and disappears. Upon the face, where the rash is most profuse, this swelling and associated œdema of the tissues results in what may amount to obliteration of the ordinary features, and the patient becomes unrecognisable (confluent smallpox). The constitutional symptoms return with great severity.

4. *Stage of Desiccation.*—The pustules gradually shrink and dry up, forming crusts or scabs which ultimately separate, leaving characteristic deep-set pocks. This stage is of variable duration. The separation of the scabs, and particularly of the "seeds" upon the palms and soles, may take three, four, or more weeks.

(*b*) *Variola minor* (alastrim) varies widely in clinical severity. Cases have occurred indistinguishable in any respect from a severe attack of classical smallpox. On the other hand, "influenza with spots" has not inaptly described most cases. Even in the unvaccinated, the prodromal illness may be trifling and the lesions very sparse. Mortality in either vaccinated or unvaccinated patients is very low. There is a tendency to prolongation of the incubation period which may extend to fifteen days to the onset of prodromal symptoms. The latter although usually slight may be severe, and in any case form no guide to the probable profusion of the eruption. Prodromal rashes are rare and, when they occur, erythematous

or urticarial. The distribution of the eruption is identical with that of ordinary smallpox. The more leisurely eruption of the papules, which may appear upon the face twenty-four hours earlier than upon the extremities, the more rapid maturation of the lesions, which may be unilocular, and the marked tendency to abort at any stage give a deceptive appearance of " cropping " which has led to confusion with chickenpox. Secondary fever is slight or absent and the incidence of complications is low. In the unvaccinated, smallpox occurs in *unmodified* form, but the attack becomes *modified* as the result of previous successful vaccination.

Modified smallpox (*Varioloid*) is clinically indistinguishable from *variola minor*. In the former, modification results from partial immunity to a virulent strain ; in the other it is due to a degraded virus.

A further classification into *discrete* and *confluent* smallpox refers to the closeness with which the lesions are set upon the *face*.

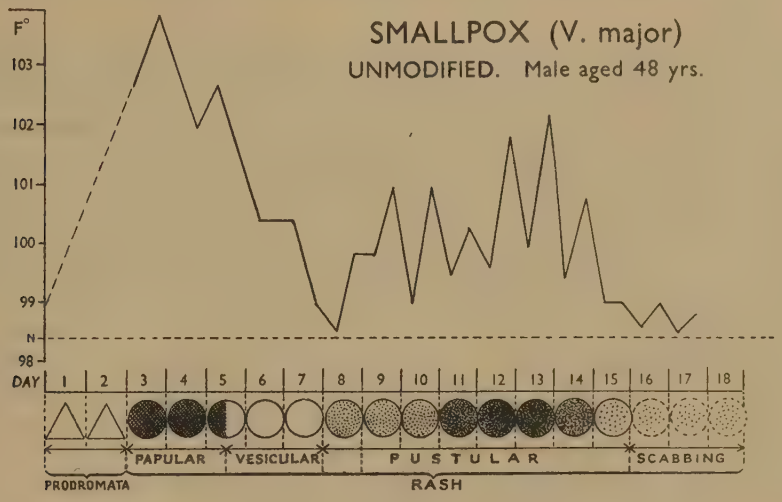

Fig. 3

Temperature chart of classical smallpox (V. major) in an unvaccinated patient aged 48.

Hæmorrhagic smallpox is characterised by the extreme severity of the prodromal toxæmia, the occurrence of petechial prodromal rashes, and of generalised erythematous rashes. Rarely death may occur from toxæmia either before the appearance of the papules or as they are appearing. The papules are poorly formed and velvety to the touch. Hæmorrhages from mucous membranes occur. Occasionally hæmorrhages are delayed until the vesicular or pustular stage.

Complications.—The important complications are the following :—

(*a*) *Cardiac.*—Myocardial failure may occur at any stage, but most commonly during the phase of pustulation.

(*b*) *Respiratory.*—Lesions occurring in the larynx may occasion œdema of the glottis. Some bronchitis is usual, and broncho-pneumonia is common.

(*c*) *Nervous.*—Transient toxic encephalitis may complicate the prodromal stage. Encephalo-myelitis, pathologically identical with post-vaccinal encephalitis (*infra*), may occur from five to thirteen days after the appearance

of the focal rash. Peripheral neuritis and psychoses are occasional sequelæ.

(*d*) *Special Senses.*—Some degree of conjunctivitis occurs in most severe cases. Keratitis, followed by ulceration and rapid destruction of the globe, with sympathetic ophthalmia of the other eye, may result in complete blindness. Otitis media, due to secondary infection, is not uncommon.

Albuminuria is constant, and suppression of urine may result in uræmia. Orchitis is an occasional complication in severe cases and produces areas of necrosis in the body of the testicle. Troublesome boils are common during convalescence.

Diagnosis.—1. *Prodromal Stage.*—Influenza is the condition most commonly confused. Other conditions causing malaise, vomiting, pyrexia, and more or less localised pain, are pneumonia and acute appendicitis. The following diseases have been diagnosed as the prodromal stage of smallpox: cerebrospinal fever, typhus, relapsing fever, plague, malaria, and heat-stroke.

2. *Eruptive Stage.*—The characteristic centrifugal distribution may be confirmed by an actual count of the lesions present upon the proximal and distal portions of a limb or of those above a line drawn at the level of the nostrils, compared with those below such an imaginary line. The characters of the individual lesions, although important, are subordinate to the crucial diagnostic test of distribution. The papule is deep-seated, and if picked up between finger and thumb it feels "shotty." The vesicle is multilocular and frequently shows umbilication. Unilocular vesicles may occur in children and in *V. minor*. Recent successful vaccination renders a diagnosis of smallpox very unlikely. Vaccination first performed in the eruptive stage will be unsuccessful.

The condition most liable to be confused with smallpox is, of course, chickenpox. In the latter disease the prodromal period is absent or of negligible severity. The rash of chickenpox also differs from that of smallpox in distribution and type (*vide* p. 42). One important point in the differentiation of the two conditions is that in chickenpox the maturation of the lesions is rapid and adjacent lesions of successive crops are in different stages of development; thus papules, vesicles, and pustules may be seen side by side on the same area of skin. This is never the case in classical unmodified smallpox, where all lesions in any particular area of skin mature concurrently. (See, however, *Variola minor* and *Varioloid*, p. 36.)

There may also be confusion between the eruption of smallpox in its early stages and that of measles. The deeply seated smallpox papules are unlike the superficial lesions of measles, in which, too, Koplik's spots are pathognomonic.

Certain eruptions may be confused with smallpox; such are acne, bullous impetigo, pustular syphilides, erythema multiforme, pemphigus, dermatitis herpetiformis, and drug rashes due to sulphonamides, bromides, iodides, and copaiba.

Complement-fixation Test.—This test, originally described by Craigie and Wishart, is most valuable. Fluid from vesicles or pustules, taken up in a capillary tube, provides sufficient material for the test, the result of which is usually available within twenty-four hours of the receipt of specimens at the laboratory (Downie). The test is now in routine use for the diagnosis of doubtful cases.

Identification of Paschen Bodies.—Van Rooyen and Illingworth have confirmed the diagnosis of variola in the papular and early vesicular stages by the identification of Paschen bodies in stained smears under the microscope. The laboratory and clinical findings agreed in 96 per cent. of seventy-seven cases. In thirty-two cases the laboratory answer was positive on the first day of the rash.

Treatment.—Vaccination during the latter part of the incubation period and in the prodromal stage may modify the attack, but in the eruptive stage it has no effect. Delirium may call for appropriate sedative treatment and sometimes for restraint, as the patient may attempt to escape. The heart must be watched throughout the attack and cardiac stimulants employed if indicated. Broncho-pneumonia needs treatment upon ordinary lines. In the case of keratitis with perforating ulcer, prompt excision of the globe may become necessary in order to prevent sympathetic ophthalmia. Sulphonamides have been used with equivocal success to mitigate the severity of the pustular stage, but must be given early and continued.

Mode of Spread and Prevention.—The virus is conveyed in the secretions of the mouth and nose, and also persists in the scabs and bedding for long periods. The disease may be spread through the air for *short* distances. The administrative control of the disease is based upon the view that aerial convection *may* occur. Although both are disseminated with equal readiness, the strain causal of *V. major*, being highly virulent, is effective in smaller doses than the degraded strain causal of *V. minor*, with the practical result that *V. minor* is less infectious. Patients must be isolated in a hospital set apart for that disease from the time of diagnosis until the scabs have completely separated, to leave healed cicatrices. All known contacts must be vaccinated or, if they refuse, be kept under observation (not necessarily in quarantine) for sixteen days. Vaccination and revaccination is the real method of prevention.

VACCINIA AND VACCINATION

In 1796 Edward Jenner of Gloucester introduced the process of *vaccination*. He noted that inoculation of human beings with the virus of cowpox " vaccination " produced a localised process which was protective against smallpox. All subsequent evidence is in favour of Jenner's belief. The virus of vaccinia " is nothing else than that of variola modified in its virulence for man, but not in its immunising action against variola, by passage through the cow " (Mervyn Gordon).

The gradual extension of compulsory vaccination during the nineteenth century resulted not only in a decline in the mortality from smallpox at all ages but in a virtual reversal of the age incidence. Instead of being predominantly a disease of childhood its maximum incidence and mortality fell upon unvaccinated or imperfectly vaccinated adults.

Compulsory vaccination, with its wide loophole for the " conscientious objector," is, in Great Britain, now more honoured in the breach than the observance and is likely to become voluntary. At the present time the community is under-vaccinated ; that widespread epidemics of virulent smallpox, in spite of numerous importations, have been obviated is due

to the vigilance of medical officers at seaports and airports and the resort to *ad hoc* mass-vaccination in the areas affected.

Prior to the Vaccination Order of 1929 it was customary to make four insertions of calf lymph in order to secure a total area of vesiculation of not less than half a square inch. While four insertions are still permissible and desirable if effective immunity for "not less than seven years" be desired, Public Vaccinators are now directed to make a *single* linear insertion with a minimum of trauma in order to reduce as far as possible local and constitutional effects and the likelihood of nervous sequelæ. Scarification and cross-hatching are to be deprecated.

Technique.—(*a*) Glycerinated calf lymph contained in capillary tubes is used. It must be stored in an ice chest until required and used within a week of receipt. (*b*) *Site.*—The left deltoid region. (*c*) *Preparation.*—The skin is washed with soap and water or gently swabbed with acetone and *allowed to dry.* No non-volatile antiseptic must be used. (*d*) *Insertion.*—The ends of the capillary tube are broken and an ejector attached. One drop of lymph (for each insertion) is blown out on to the skin. Thereafter, the lymph may be inserted either by means of a linear scratch (the standard method for Public Vaccinators) or by the newer American multiple-pressure method. A sterilised Hagedorn needle is suitable for either technique. (i) *Scratch Method.*—With the point of the needle a superficial scratch is made, without drawing blood, through the drop of lymph. The length of the scratch, as officially advised, should be $\frac{1}{8}$ in., but must not exceed $\frac{1}{4}$ in. *This single insertion is not to be relied upon during prevalence of V. major; three linear insertions of $\frac{3}{4}$ in. give the requisite protection.* (ii) *Multiple-pressure Method.*—Using the side of the needle-point, "pressures" are applied through a very small drop of lymph by moving the needle up and down "with enough force to demonstrate the elasticity of the skin, but not so vigorously as to draw blood" (Parish), over an area of $\frac{1}{8}$ in. For the primary vaccination of infants 30 pressures are used, but for children and adults 6 to 10 only, owing to the possible risk of encephalitis. For all secondary vaccinations 30 pressures are used. After exposure to smallpox multiple vaccinations—30 pressures at more than one site—are advised. The advantages claimed are less severe reactions, smaller scars, more rapid technique, virtually intact epidermis, and therefore less risk of septic infection (Parish). (*e*) *Dressing.*—The insertion is allowed to dry *thoroughly.* A simple dry dressing is then applied and secured by a bandage. (*f*) *Inspection.*—The arm should be inspected on the seventh or eighth day and again on the fourteenth or fifteenth day.

The course of a successful primary vaccination is as follows: (i) there is an incubation period of *three days*, during which itching and irritation are common; (ii) on the fourth day a papule appears at each insertion; (iii) on the fifth day the papule becomes a vesicle surrounded by an areola, and the vesicle during the ensuing twenty-four hours shows umbilication; (iv) during the seventh and eighth days the vesicle becomes opalescent, the areola increases in intensity, and there is much infiltration of the whole site; (v) from the eighth to the tenth day definite pustulation of each lesion occurs, with an associated enlargement of the axillary glands. The arm may become quite "brawny," as in cellulitis. Constitutional symptoms, of varying severity, are met with. Transient splenomegaly occurs in a proportion of cases. From the tenth day onwards the pustules gradually

dry up to form scabs, which ultimately separate, leaving scars at first pink, but later white and exhibiting pitting or *foveation*. This *foveated* scar is the essential sign of a successful vaccination.

Revaccination.—Unless a very long period has elapsed since the primary operation, the local and general signs and symptoms which follow a revaccination are usually considerably modified and accelerated. Failure to "take," or the appearance merely of a small papule which aborts, should not be accepted as evidence of immunity, especially if there has been exposure to smallpox. The operation should be repeated at least once with lymph of known potency (Marsden). The lesions may abort at any stage. Revaccination should be carried out every seven years, or even more frequently in the case of persons living in countries where smallpox is endemic.

Generalised Vaccinia very occasionally occurs. It is characterised by the eruption of papules upon the body at any time during the phase of activity of the local lesions, *i.e.*, from the fourth to the tenth day. The papules appear in crops and go through the stages of vesiculation and pustulation. Treatment with convalescent vaccinia serum has been successful.

The appearance of lesions elsewhere than upon the arm may be due to the accidental transference of lymph by the patient, after scratching the arm, into an abrasion upon the face or elsewhere.

Complications.—These are usually due to sepsis introduced by the patient as the result of scratching. Erysipelas may occur in this way. Infection with syphilis or tubercle is an absolute impossibility as the result of vaccination with calf lymph, but it was possible in the old days of arm to arm vaccination, which is now never employed.

Post-vaccinal Encephalitis.—Encephalitis or meningo-encephalitis following vaccination is of rare occurrence. The symptoms and histological lesions appear to be identical with those of encephalitis associated with other of the acute virus infections, *e.g.*, measles. Most of the recorded cases have occurred following primary vaccination in children of *school age*. Cure has followed the injection of convalescent vaccinia serum (obtainable from the Government Lymph Establishment). Simultaneous injection of parental whole blood has been practised. Horse anti-vaccinial serum has also been used.

Duration of Immunity.—The duration of immunity is believed to be directly proportional to the area of true foveated scarring, and when this area measures not less than half a square inch immunity may be valid for seven years; but, in the event of exposure, no risks must be taken. Whatever the alleged date of the last vaccination and the area of scarring, unless this is manifestly recent it is wiser to revaccinate. If immunity, following primary vaccination, has waned, an attack of smallpox is usually mitigated and modified.

Vaccination, performed subsequently to infection with smallpox and up to the date of onset of symptoms, will "take" and pass through its typical course. Protection is afforded by vaccination performed within three days of infection, but this may not be absolute in those vaccinated for the first time; the course of the disease, however, will usually be mild. Vaccination may mitigate the severity of the disease when performed at any time after infection up to the onset of the eruption.

CHICKENPOX

Chickenpox (*Varicella*) occurs all over the world, chiefly in localised epidemics in schools and children's institutions. The disease is most prevalent in the winter months. Chickenpox and smallpox may be prevalent together. The virus is an elementary body analogous to, but quite distinct from, the Paschen bodies of smallpox. Though chiefly a disease of childhood, chickenpox attacks adults, and second attacks, though rare, are occasionally seen.

Incubation Period.—From fourteen to twenty-one days.

Clinical Description.—In children, the prodromal period may be absent or confined to slight pyrexia and increase in pulse-rate ; adults, however, may exhibit prodromal symptoms such as malaise, nausea, and pain in the back for a period of twenty-four hours or, rarely, longer, before the eruption appears. There is occasionally a prodromal rash of scarlatiniform type. The lesions appear in from three to five crops over a period of two to four days. Initially macules or maculo-papules, they become, within a few hours, clear, well-filled superficial vesicles, some of a typically elliptical shape. In twenty-four hours the vesicles assume a pale yellowish opalescent appearance and become flaccid pustules. Ultimately, scabbing and separation take place. Shallow, pinkish depressions which form white cicatrices are left. Owing to the fact that the lesions appear in crops and that the cycle of the individual lesions from papule to scab is a short one, lesions in various stages of development are present upon the skin after the first twenty-four to thirty-six hours. The eruption probably always first appears within the buccal cavity, but the lesions here are so delicate that they readily rupture and may not be recognisable. They may occur within the larynx and upon the conjunctiva. Upon the skin they first appear upon the back, chest, and abdomen—particularly the lower abdomen—and the adductor aspects of the thighs. The face and hairy scalp are next invaded. The arms and legs, including sometimes the palms and soles, are usually the last to present lesions.

The distribution as a whole is centripetal, being most abundant upon the trunk. The numbers of lesions upon the upper arms exceed those upon the forearms ; the numbers upon the thighs, those upon the legs. The lesions of chickenpox, in contrast to smallpox, tend to invade concavities and protected areas such as the axilla.

Herpes and Varicella.—The virus of chickenpox, ordinarily dermatotropic, occasionally assumes neurotropic properties resulting in the clinical manifestations of herpes zoster. This is not to say that herpes zoster is invariably due to the virus of chickenpox. Herpes zoster and chickenpox may occur concurrently in the same patient.

The exceptional occurrence of *encephalitis* provides further evidence of the neurotropic affinities of the virus.

Complications.—The occasional occurrence of vesicles within the larynx has been noted. Very rarely this localisation has necessitated tracheotomy. Lesions upon the conjunctiva, being quite superficial, rarely give rise to trouble. In debilitated children the lesions may ulcerate or become gangrenous. *Varicella gangrenosa* may be caused by the infection of the lesions with hæmolytic streptococci or virulent diphtheria bacilli, giving rise to early fulminating and late subacute forms respectively. Diphtheria and

scarlet fever antitoxins and sulphonamides or penicillin should be given as soon as possible in all cases of *V. gangrenosa*.

Diagnosis.—If the points noted under clinical description are carefully compared with the description of smallpox, confusion between the diagnosis of the two diseases should not arise. The prodromal scarlatiniform rash is sometimes diagnosed as scarlet fever. Papular urticaria, the lesions of which never appear in the mouth, scabies, and impetigo have also to be excluded.

Treatment.—Bed and light diet for a few days are desirable. It is important to prevent undue scarring, either as the result of scratching the lesions or of secondary impetigo. Small doses of the sulphonamides, given early in the attack, may reduce the severity of pustulation. Separation of the scabs is facilitated by treating each with carbolised oil applied gently with a feather.

Mode of Spread and Prevention.—The disease is extremely infectious in its earliest stages. Infectivity wanes rapidly after the full appearance of the eruption, but isolation should be maintained until all the scabs have separated. Infection is commonly conveyed from person to person ; in the early stages the virus is readily carried upon the hands of a third person who has been in attendance. There is evidence that in its most infective phase chickenpox may be spread for short distances, as from bed to bed, through the air. Prevention consists in the earliest possible isolation of cases, concurrent and terminal disinfection, and an observation period of twenty-one days for exposed non-immune children.

TYPHOID AND PARATYPHOID FEVERS

(*Enteric Fever*)

Ætiology.—Typhoid and paratyphoid fevers (A, B, and C), the diseases which comprise the " enteric group," occur all over the world and affect all races. Of the paratyphoids, B is more common in England ; in the East, A is more frequently encountered ; C is of exceptional occurrence. The prevalence or otherwise of enteric fever in any country, district, or town is an index of the general standard of sanitation, particularly in relation to the water supply. In this country the number of notifications of enteric fever varies considerably in individual years, *e.g.*, 1,200 in 1934 and 2,500 in 1936. These figures are small compared with those obtaining in the past ; even as recently as 1911 there were some 13,800 notifications. " The major causes such as polluted water supplies and urban environment are gradually being eliminated and there now remain the more elusive and less easily controlled factors such as carriers, contact infection, contaminated shell fish and other foods " (G. Newman).

Localised epidemics occur from time to time and an increase in the notifications in any year may be due, almost entirely, to a single outbreak. In outbreaks of typhoid inquiries should first be directed to the water supply, next to milk. Shell fish (oysters and mussels) and watercress are now uncommon sources. Epidemics of paratyphoid are very rarely water-borne and are usually traceable to a carrier, but, even so, a carrier may be the primary source of infection. Infection with bacilli of the enteric group may be indirect, through articles of food or drink, whether these have been infected through the medium of sewage, flies, or carriers, or direct, as happens

when a nurse infects herself with the dejecta of a patient suffering from the disease.

Carriers.—Persons who have had a recognised or unrecognised attack of the disease may continue to excrete organisms in the fæces, usually intermittently, for many years. The bacilli persist in the gall-bladder and pass thence into the intestine. Biliary carriers are usually women, and, having regard to their closer association with the preparation of food, are the more dangerous. Urinary carriers also occur. Sulphathiazole will sometimes cure the urinary carrier, but the biliary carrier is refractory and may require cholecystectomy. There is laboratory and clinical evidence that sulphathiazole combined with massive doses of penicillin may prove more successful (*vide infra* Treatment). By means of Vi-bacteriophage, typing the detection of carriers responsible for outbreaks has been much facilitated.

Typhoid fever shows distinct seasonal incidence. In Great Britain prevalence commences in September and attains its maximum in October and November ; fewest cases occur in the spring. In warm climates the greatest number of cases occur during the hot weather. The seasonal incidence of paratyphoid fever is less evident.

All ages are liable to attack by infections of the enteric group, but the period from ten to thirty-five provides the greatest number of cases.

The fatality rate from typhoid varies from 10 to 20 per cent. ; for the paratyphoids it ranges from 1 to 9 per cent.

Bacteriology.—The typhoid-paratyphoid bacilli belong to the *Salmonella group* and have the following characteristics : they are motile and, with suitable staining, can be shown to possess flagella. They are gram-negative, and in culture they do not ferment lactose. Differentiation between the various types depends on cultural and agglutination reactions. The bacilli occur in the blood in the early stages particularly ; in the rose spots, the fæces, urine, and internal organs, especially the spleen and gall-bladder.

Pathology.—Except that the intestinal lesions caused by the paratyphoid bacilli are as a rule less severe than those due to *Bact. typhosum,* and that in paratyphoid infections the large bowel shows ulceration more commonly than in typhoid, the pathology of the conditions is the same. The typical lesions occur in Peyer's patches, which undergo progressive inflammatory changes resulting in ulceration and sloughing. The detachment of the slough may cause either hæmorrhage or perforation of the bowel, but the usual process is granulation and healing. The ulcers which occur are elliptical, with their long axes in line with the length of the intestine ; the edges are undermined and the bases clean ; there is associated enlargement of mesenteric glands. The spleen is enlarged and friable and teems with the specific organism. The liver and myocardium show degenerative changes. Patches of Zenker's degeneration may affect the large muscles. Suppurative arthritis and abscesses in the long bones occur, from either of which the specific organisms may be recovered. The so-called " typhoid spine " is a periostitis of the bodies of the vertebræ with associated changes in the intervertebral discs.

Blood Picture.—Typically, leucopenia with eosinopenia occurs after the first few days, and may be an important accessory factor in diagnosis in the absence of bacteriological or serological facilities. Complications due to secondary infections during the course of the disease give rise, unless the patient's condition be very grave, to a polymorphonuclear leucocytosis.

Incubation Period.—In both typhoid and the paratyphoids the incubation period is variable ; that of typhoid varies from twelve to sixteen days, but exceptionally long periods exceeding twenty days are on record. The paratyphoids have even more variable incubation periods, ranging from five to fifteen days.

Clinical Description.—Typhoid and the paratyphoids possess great clinical similarity, but show certain more or less characteristic differences.

Typhoid.—The onset is usually insidious ; so insidious in some cases (ambulant forms) that the patient may walk about for days while actually suffering from the disease, until he is incapacitated by the gradual advance of the infection, or overtaken by some sudden calamity such as a hæmorrhage or myocardial failure. In those who have undergone protective inoculation, but in whom immunity has to a great extent waned with the lapse of time, the disease may be mild or abortive. Such mild types also occur in children.

Typhoid fever of average severity shows three fairly well-marked stages :—

First Stage.—This period is characterised by gradually advancing general

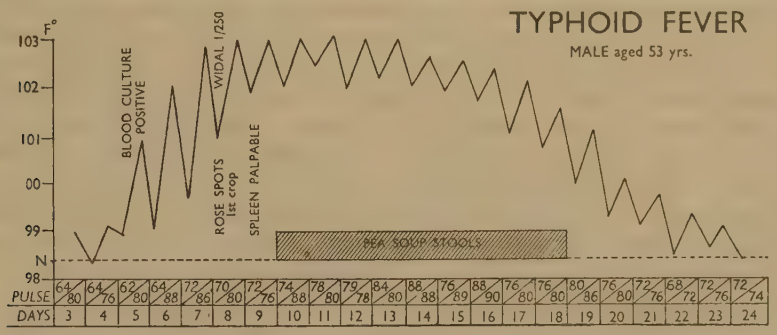

Fig. 4

Temperature chart of typhoid fever. Male—53 years : uncomplicated attack of average severity.

malaise and a desire for sleep, although sleep is disturbed. There is headache, which is usually frontal and often extremely severe, giddiness, pains in the limbs, and sometimes in the right iliac fossa ; anorexia and thirst ; nausea and vomiting, which, however, are relatively uncommon. The tongue is dry and furred, and the bowels are usually constipated at the onset. Epistaxis is not uncommon.

During the period of invasion, which lasts from five to seven days, the temperature rises by about a degree each evening, until by the end of the first week it has usually attained 103° to 104° F. The temperature chart in enteric is often described as having a step-ladder character during the first week.

Second Stage.—By the end of the first week the general symptoms have advanced and the patient presents a characteristic appearance. Markedly prostrated, he is inert and may be stuporous ; muttering delirium may be present, particularly at night ; he has lost flesh ; the tongue is dry and brown and there are sordes around the lips ; the abdomen is distended. The pulse is now soft, tends to be slow in proportion to the temperature, and is often dicrotic.

At the end of the first week the eruption of " typhoid spots " occurs.

These are discrete lenticular erythematous rose spots, which usually are seen upon the upper abdomen and upon the back. In number, they may be confined to half a dozen and require careful search. The most important characteristic of the "rose spot" of typhoid is its transitory nature; an individual spot is seldom visible for much over forty-eight hours, after which time it fades. Fresh crops of spots may continue to appear for as long as several weeks. If in a suspected case of enteric doubtful spots be seen, they should be ringed round with indelible pencil, so that at a later visit their presence or absence may be confirmed. By the end of the first week also the spleen has often become palpable. The typhoid patient may remain constipated throughout, but usually initial constipation is succeeded during the second week by diarrhœa. The stools in typhoid are typical—the so-called "pea-soup" stools. They are liquid and of a pale yellow colour, containing shreds of mucus, and are alkaline in reaction. Owing to the presence of the specific micro-organism in large numbers, the fæces, or articles of bed-clothes contaminated by them, are highly infective. During the course of the second week the stools become more numerous, and sometimes twenty or more may be passed in the twenty-four hours. Meteorism may be troublesome. The urine is diminished in quantity during the height of the disease; its specific gravity may be high, and the reaction is acid. Albuminuria occurs in a proportion of cases. The chlorides are diminished. Most characteristic is the high degree of *indicanuria* which occurs. *Bacilluria* is not uncommon. A certain degree of *bronchitis* may be regarded as normal in typhoid. In severe cases the patient gradually sinks into a "typhoid state," and may die from asthenia. The typhoid state is characterised by extreme prostration; incontinence of urine and fæces is frequent, retention of urine less so. The patient is stuporous during the day; delirium, which is always more evident at night, is usually of the muttering type, but may be violent, necessitating restraint. Muscular tremors affecting the hands, tremors of the lips and the tongue, which may be difficult to extrude owing to its parched state, also occur. The patient slips down in the bed, plucks at the bedclothes, and gropes for non-existent objects. The *facies* is characteristic; the features are pinched and drawn; an irregular bright flush occurs upon the cheeks; the eyes are sunken and the pupils dilated. Hiccough may be troublesome. The patient may sink into a state of coma-vigil, and die from myocardial failure.

In the case of average severity, after about two weeks of sustained pyrexia, the patient enters the third stage.

Third Stage.—This is the period of decline of the disease, characterised by general physical and mental improvement. The temperature falls usually by lysis and rarely by crisis; the stools become less frequent and semi-formed or constipation may ensue. Urine is passed in normal quantity. The tongue cleans and appetite returns. Abdominal distension disappears and the spleen is no longer palpable. The patient is mentally clear and sleeps and eats well.

This period of decline may be interrupted by *recrudescence*. All the symptoms return, and the patient is again in peril. Otherwise, the period of decline merges into that of convalescence, which may be quite uneventful or may be terminated by a *relapse* after a varying apyrexial period. Relapses, more than one of which may occur, are usually, but not always, less severe than the initial attack. All the symptoms and signs of the first attack,

including the rose spots, are reproduced. *Second attacks* may occur at an interval of years after the first, but are rare. A clinical recrudescence or relapse may, however, be due to an extraneous infection, *e.g.*, the pneumococcus.

Paratyphoid.—Apart from the somewhat shorter incubation period, the paratyphoids show certain other differences. It is impossible to discriminate clinically between paratyphoids A, B, and C. The paratyphoids may have a gradual onset like typhoid, but usually it is much more abrupt. Particularly in para. B. a gastro-intestinal type of onset may occur, with a sudden attack of colicky abdominal pain, diarrhœa, and vomiting. There is intense headache, which may continue throughout the attack, and early prostration. The temperature rises rapidly to 101° F., but pyrexia in the paratyphoids, especially in para. B, is usually of shorter duration than in typhoid. In para. B the attack may be of only a week or ten days' duration, or may extend to eighteen days ; in para. A the typical attack extends over three weeks. In both, the temperature chart exhibits a " spiky " character

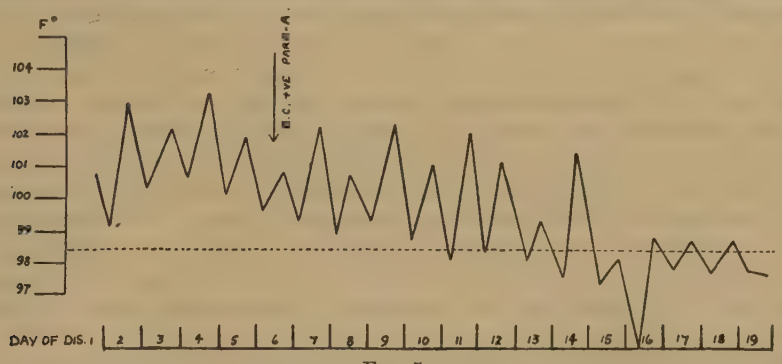

Fig. 5

Temperature Chart of a Paratyphoid A Fever.

Male—28 years. Blood culture positive on sixth day of disease. Duration of attack nearly three weeks. Patient constipated throughout. The chart shows the typical remittent pyrexia of paratyphoid fever.

with a range of some two degrees between morning and evening temperature. Bradycardia is more common than in typhoid. The rash in the paratyphoids appears in crops, and is characteristically much more abundant, especially in para. A, than in typhoid. It may invade the face. The spots may also be larger and of a deeper colour ; in para. B they may be papular. Constipation is common in the paratyphoids. Para. C may resemble the ordinary paratyphoid ; the onset may be of the gastro-intestinal type, but acute septicæmic, bronchitic, and pneumonic forms have been recorded.

Types of Enteric Fever.—Typhoid, and much more rarely paratyphoid, may occur in a fulminating, hyperpyrexial form, death taking place from toxæmia in a few days. Hæmorrhagic typhoid is very rare and is almost invariably fatal.

Typhoid or paratyphoid may commence with meningism or with true acute meningitis, the specific organisms, in the latter case, being recoverable from the cerebrospinal fluid. In infants and young children the onset of enteric fever is frequently abrupt and may simulate the " acute abdomen." Particularly in para. B, meningitis, gastro-enteritis, or broncho-pneumonia may in infants dominate the clinical picture in the early stages.

Complications.—These are numerous. Any of them may occur in both typhoid and the paratyphoids, although they are, upon the whole, much more likely to do so in the case of typhoid fever.

The major complications are most liable to occur from the end of the second to the end of the third or beginning of the fourth week. The two gravest of these are *hæmorrhage* and *perforation*, caused by the separation of the sloughs from ulcerated Peyer's patches. In the process of separation a vessel may become eroded, or a tear occur through the tissue remaining at the base of the ulcer and through the peritoneal covering of the bowel. *Myocarditis*, which is usually marked during the third week, is the result of toxæmia. *Lobar pneumonia*, whether it occurs, as it may do, at the onset, or, more usually, during the third week, is due to a secondary pneumococcal infection, although typhoid bacilli may be present in the sputum. *Broncho-pneumonia* is not an infrequent terminal event, superimposed upon hypostatic *congestion*.

Hæmorrhage, perforation, and myocarditis must be further discussed.

Hæmorrhage.—Small streaks of blood may be observable in the stools during the first week, as the result of the hyperæmic condition of Peyer's patches. They are of no importance. At any time after the end of the second week, and particularly at the end of the third week, hæmorrhages of considerable magnitude may occur quite suddenly. The patient complains of faintness and of abdominal discomfort rather than pain ; he becomes pale, and sweat may appear upon the forehead. He may be restless with sighing respirations, and vomiting sometimes occurs. The pulse becomes thready, rapid, and running, and the temperature falls to subnormal. The blood passed per rectum may be bright red or dark, depending on the length of time it has remained in the intestine. Hæmorrhages may be single or repeated.

Perforation.—Perforation may be associated with or follow hæmorrhage, or it may occur independently. Though usually single, perforations may be multiple. The most common site for their occurrence is from 1 to 2 ft. from the ileo-cæcal valve. Although perforation is usually a complication of a severe attack, or one which has shown recrudescence, it may also occur in a mild attack. The majority of perforations occur at the end of the third week. The patient suddenly complains of acute pain in the lower abdomen, particularly in the right iliac fossa. The facial expression becomes anxious and drawn ; there may be beads of sweat upon the forehead. The pulse and respirations increase and the temperature may show a sudden drop, though this is by no means invariable. A rigor sometimes takes place. Vomiting at this stage is uncommon. There is great tenderness upon palpation of the lower abdomen, and the abdominal muscles are " on guard." These are the early symptoms and signs of perforation ; later, signs of general peritonitis appear. Disappearance of the liver dullness, which used to be described as one of the cardinal signs of perforation, is both inconstant and late. To await it is seriously to diminish the patient's already slender chance of recovery.

Myocarditis.—Although cardiac involvement may manifest itself at any stage, it is particularly liable to do so during the third week. The signs and symptoms do not differ from those of toxic myocarditis due to any other infection. Peripheral circulatory failure is an important associated factor in the severe case and may determine the issue.

Many other complications are occasionally encountered. Perhaps the most frequent is *phlebitis* of the left femoral vein, which leads to a femoral thrombosis during the later stages of typhoid or in early convalescence. Rarer complications are the following: pericarditis and endocarditis, cholecystitis, ulcerative laryngitis. *Parotitis*, which is usually suppurative, and *orchitis* are not very uncommon. *Appendicitis*, with which perforation may be confused, is an occasional complication. *Otitis media*, *osteitis* of the long bones with abscess formation, *myositis*, resulting in rupture and ecchymoses due to hæmorrhages, are all complications which occur in the later stages or during convalescence. Spondylitis ("Typhoid Spine") has already been mentioned (*vide* p. 44).

Associated Diseases.—Double infections of typhoid and paratyphoid occur. In the tropics the water which has caused typhoid may also contain the organisms of other water-borne diseases, and these may occur together with typhoid, or rather, since the incubation periods are shorter, precede it in the same patient. Double infections of cholera and typhoid and bacillary or amœbic dysentery and typhoid are encountered. Attacks of malaria or relapsing fever during the course of typhoid sometimes occur. Diphtheria is not uncommon in association with typhoid or paratyphoid.

Sequelæ.—Mental dullness may persist for a long period after the attack, and occasionally true psychoses result. Various organic nerve lesions have been recorded. Chronic cholecystitis is an important sequel, as it may be associated with a carrier state. Bone abscesses may make their first appearance years after the attack. Alopecia, particularly in children, may be an unsightly sequel.

Diagnosis.—The diagnosis of typhoid or paratyphoid is seldom more than suspected on clinical grounds during the first few days. Many other acute infections may give rise to error, such as pneumonia, influenza, smallpox, cerebrospinal fever, typhus fever, malaria, undulant fever either of the melitensis or abortus type, miliary tuberculosis, and tuberculous meningitis. Suspicion of the nature of the condition will be aroused if the history, the mode of onset, and the symptoms, which have already been described, are carefully weighed. Considerable assistance will be afforded by the character of the temperature chart. In the paratyphoids early diagnosis may be even more difficult, especially in the mild forms and in those with a gastro-intestinal onset. After the first week the persistence of the symptoms, the appearance of the spots, the palpable spleen, and the passing of the typical "pea-soup" stools should make clinical diagnosis possible.

Laboratory Diagnosis.—Three laboratory tests are available.

1. *Blood Culture.*—A large proportion of positive results may be obtained if blood culture be performed during the first week of enteric. This procedure should always be adopted after four days of pyrexia when there is any suspicion of enteric. At least 5 c.c. of blood, collected under strictly aseptic conditions, should be introduced at once into bile salt medium and sent to the laboratory for incubation.

2. *Agglutination Tests* (*Widal and Felix Modification*).—Agglutinins in sufficient quantities to produce a positive Widal test appear in the blood serum within eight to fourteen days of the onset.

The antigenic structure of each organism is complex; at least three types of agglutinins appear, distinguishable by the rate of clumping and

its form : (i) *Somatic* (*O-agglutinins*) ; their appearance is indicative of an active infection. (ii) *Flagellar* (*H-agglutinins*), *type specific* ; provide information as to the particular organism responsible. (iii) *Group agglutinins* (also *flagellar*) are common to all Salmonella organisms *except* typhoid. Their presence is indicative of a Salmonella infection, but gives no information as to the particular organism responsible. The Felix modification of the Widal test involves testing for these different agglutinins. In *typhoid* fever a *Vi-agglutinin* (indicative of virulence) is described by Felix. For *Bact. typhosum* and *paratyphosum A and B*, the following titres are in each case diagnostically significant : H, 1 in 30 ; O, 1 in 50 (Felix).

In those who have previously been inoculated with typhoid-paratyphoid vaccine (T.A.B.C.) a single test is of little value in detecting the presence of an active infection. Most information is obtained from a rising titre of O-agglutinins, since, in the inoculated, H-agglutinins may rise during any febrile illness (*Anamnestic reaction*).

3. *Examination of Stools and Urine.*—The specific organisms by the use of highly selective culture media may, in the case of *Bact. paratyphosum-B* at least, be recovered from the stools in a high proportion of cases during the first week of the illness. They are still more likely to be isolated from *both* stools and urine during the second week and onwards.

Treatment.—The treatment of typhoid may conveniently be considered under the following headings : (1) general, (2) dietetic, (3) symptomatic, (4) specific, and (5) chemotherapy.

1. *General.*—Absolute rest is imperative from the earliest possible moment until the temperature has remained normal for at least ten days. Excluding diphtheria and typhus, there is no acute infection in which limitation of movement upon the part of the patient is so essential. This is not the same thing as saying that the patient must not be moved. Preferably nursed upon a sorbo-rubber bed, the patient's posture must be skilfully changed by the nurse at fairly frequent intervals during the twenty-four hours, lest pressure-sores result. These may readily occur and are a serious complication. Sudden movements by the patient and abrupt movement of the patient by the nurse must be avoided.

2. *Dietetic.*—The next essential is a suitable diet. The practice is to allow typhoid patients, even during the acute stages of the disease, a high-calorie diet, including such articles of food as thin bread and butter without crust, minced meat, and pounded fish. Mashed potatoes, custards, junkets, and eggs, either raw or soft-boiled, are also permissible. In severe cases with digestive disturbances the basis of the diet must be milk, *supplemented by ample quantities of water*. " Milk " is understood to include such variations in flavouring and later slight thickening as may be devised to relieve the monotony. The patient should consume, in small amounts at a time, not less than three pints of milk in the twenty-four hours. Lemon water, weak tea and coffee may be allowed. Small amounts of milk chocolate are well tolerated, especially by children. Meat juice or extract may be given to add variety. The patient should be encouraged to take large quantities of fluids, and to these plenty of glucose should be added. This form of carbohydrate is better tolerated than is ordinary cane sugar, which in large amounts is liable to cause nausea.

There is no evidence that a liberal diet increases the risk of hæmorrhage or of perforation, while it certainly helps to maintain the patient's strength

and to shorten the period of convalescence. While the juice of fruits, such as oranges or lemons, is beneficial, it is most important to prevent the patient from eating those portions of fruit which contain much unabsorbable cellulose. There is little point in giving alcohol as a routine. If its administration be considered advisable to tide over a period of great weakness, a dry champagne is the most suitable form to employ.

Apart from the effects of the disease itself, a milk diet tends to produce a furred tongue and an unwholesome condition of the mouth. Frequent cleansing of the tongue, teeth, gums, and lips is necessary.

3. *Symptomatic*—(*a*) *Reduction of Pyrexia.*—This is best attained by means of warm or tepid sponging. The more drastic methods of packs and baths should be avoided. The sponging must be carried out as expeditiously and with as little disturbance of the patient as possible. Antipyretic drugs must be avoided, as most of them depress the heart.

(*b*) *Abdominal Distension* is best minimised by careful regulation of the diet. Intestinal antiseptics such as betanaphthol and salol possess no real value. The same may be said of hexamine, which, moreover, may produce cystitis.

(*c*) *Hæmorrhage.*—Absolute quiet should be secured. If syncope threaten, the foot of the bed should be raised upon blocks. A starch and opium enema is sometimes of value in mild cases, but for severe hæmorrhage morphia in a dose of $\frac{1}{4}$ gr. is necessary. In severe collapse, blood transfusion is required ; for cardiac failure, nikethamide (coramine) should be injected.

(*d*) *Perforation.*—Treatment is surgical, and its success depends almost entirely on early diagnosis. If operation be delayed for over twenty-four hours, death is almost invariable. Even under favourable circumstances, the mortality of perforation is over 50 per cent.

(*e*) *Circulatory Failure.*—This is in part myocardial and in part peripheral. The foot of the bed should be raised and a radiant heat cradle used. Cardiac stimulants and a transfusion of blood plasma must be given.

Careful watch must be kept for retention of urine, which must be treated by catheterisation. Other complications must be treated as they arise.

4. *Specific.*—Promising results have attended the use of Felix's " Vi-serum " which contains antibodies to the so-called " O " and " Vi " antigens of *Bact. typhosum* (not *Bact. paratyphosum*, be it noted). The serum must be given repeatedly and in full doses early in the attack, intravenously if this is severe.

5. *Chemotherapy.*—The sulphonamides have not proved of value in the enteric fevers except perhaps for bacilluria. Although the causal organisms are relatively insensitive to penicillin, McSweeney reports promising results from a combination of sulphathiazole and massive doses of penicillin, as suggested by the laboratory findings of Biggar.

Mode of Spread and Prevention.—It has already been pointed out that enteric infections are derived indirectly from contaminated water supplies, milk or food, or directly from a case of the disease or a carrier.

In most cities and towns in civilised countries the water supply and the system of sewage disposal are satisfactory. In villages, cesspools still persist which may contaminate, by leakage and percolation, the wells from which drinking water is drawn, especially if these be in the chalk. Doubtful water supplies must be chlorinated. Milk should be efficiently pasteurised. The breeding places of flies, such as stable manure, must be dealt with,

and all food must be kept covered. The search for and segregation of carriers until they are bacteriologically free, or failing this, their continued supervision, is important. The persistence of Vi-agglutinins is presumptive evidence of an active carrier-state—even if stools and urine are bacteriologically negative at the time of examination. The individual case of typhoid must be segregated until at least three consecutive specimens of urine and fæces have been shown to be bacteriologically free, or until Vi-agglutinations are no longer present in the blood. Disinfection of the stools and urine of the patient before disposal, and of linen and garments before being sent to the laundry, is imperative. Special precautions must be taken by nurses; the nails must be kept short; on no account must food or drink be taken before the hands have been well scrubbed, and then never in the environment of the patient. They should also be protected by inoculation.

Inoculation is also essential for those living in localities where the disease is prevalent and for troops proceeding abroad. The vaccine is a mixture of *Bact. typhosum* and *Bact. paratyphosum* A, B, and C (T.A.B.C.). The strains now used are alcohol killed and rich in Vi antigens; these provoke the best and most lasting antigenic response.

The mixed vaccine contains in 1 c.c. 1,000 million *Bact. typhosum* and 500 million of each of the *Bact. paratyphosum*. Two doses are given at an interval of three weeks, the first of 0·25 c.c. and the second 0·5 c.c. A further injection should be made a year later if the person is still at risk.

CEREBROSPINAL FEVER

(*Epidemic Cerebrospinal Meningitis: Spotted Fever*)

Ætiology.—Cerebrospinal fever is caused by the *Neisseria meningitidis* (meningococcus). The organism is disseminated by droplet spray, and this is particularly liable to occur under conditions of overcrowding, especially in sleeping quarters, as in dormitories and barracks. Formidable epidemics tend to appear during war, as in 1915-17 and in 1940. In England and Wales 3,712 cases were notified in 1915 and 12,771 in 1940; but, whereas the case fatality rate in 1915 was 59 per cent. at all ages, in 1940 it was 20 per cent. This fall was chiefly due to chemotherapy, since there was no indication in 1940 of a less severe clinical type. In the inter-epidemic phase the disease is represented by sporadic cases of the posterior basic type among infants and young children, the sources of infection being mild unrecognised cases and healthy carriers.

Glover has shown that a wave of high (non-contact) carrier rates precedes and accompanies an epidemic. Both contact and convalescent carriers occur and the carrier state tends to be prolonged by an unhealthy condition of the nasopharyngeal mucosa. Although sporadic cases may occur at any season, epidemics usually commence in winter and spring when catarrhal states are prevalent and propinquity is greater in degree. Indeed, some have maintained that epidemics really consist of epidemic nasopharyngeal catarrh with occasional complicating meningitis, and that there is thus a meningococcal nasopharyngitis as distinct from the carrier state. The term cerebrospinal fever implies an invasion from the nasopharynx of the blood stream followed by a localisation of the organism upon the meninges.

In the inter-epidemic phase the greatest incidence of the disease is

among children under five and especially under three, but during epidemics as might be expected from the age groups of those chiefly at risk, incidence also falls heavily upon adults up to the age of forty-five.

As already indicated, chemotherapy has transformed prognosis at all ages ; whereas the posterior basic type might have a fatality rate of 75 per cent., this is now capable of reduction to a quarter of that figure. At all ages, among cases effectively treated in hospital with the sulphonamides, the fatality rate now ranges between 9 and 10 per cent.

Bacteriology.—The *Neisseria meningitidis* (meningococcus) is a gram-negative diplococcus resembling the gonococcus ; it dies rapidly outside the body unless kept at blood heat, a point of practical importance in the collection of specimens for laboratory examination. It occurs in the naso-pharynx of carriers and in the cerebrospinal fluid of cases of the disease ; it may also be recovered from the blood and, in certain cases, from the joints.

Meningococci conform to one of four types arranged in two groups. For serum therapy, prior determination of the group was important ; but since the sulphonamides have displaced serum and are equally effective against Group I. and II. organisms, grouping, based upon agglutination reactions, has lost its clinical significance.

Pathology.—The distinctive lesions affect cerebral tissues. Pus occurs in the pia-arachnoid mesh (subarachnoid space) and is most evident at the base, over the cerebrum and in the fissures, around the cerebellar vessels and down the posterior aspect of the spinal cord. The cerebral substance is soft and may show hæmorrhages ; the ventricles contain some excess of turbid fluid. In those who have died at a later stage, and particularly following the posterior basic form in infants, varying degrees of hydrocephalic distension and thinning of the ventricular walls may be seen. The choroidal plexus shows engorgement. Pus may be found at autopsy in the pericardium and in the joints ; frequently there are small septic foci in the kidneys. Myocardial degeneration is common but endocarditis is rare.

Incubation Period.—In the *epidemic* form the period is from one to three days ; in the *sporadic* form, from four to five days.

Clinical Description.—Cerebrospinal fever implies two pathological processes : meningococcal septicæmia and meningococcal cerebrospinal meningitis. Septicæmia may occur without meningeal involvement ; it is then only to be differentiated from septicæmias due to other organisms by the results of blood culture. Septicæmia precedes meningeal localisation of the organism and may dominate the clinical picture, as in the fulminating type of the disease, where death takes place before the full development of meningitis ; it may play an important part in the symptom-complex, the signs and symptoms of meningeal involvement being complicated by a coexistent septicæmia ; or it may be transient, and succeeded by a clinical picture which is due to meningitis alone.

The epidemic form of the disease in adults may be classified into the following clinical types : (i) fulminating ; (ii) hyperacute ; (iii) acute ; (iv) subacute or mild. These types vary in severity, but do not form well-defined groups. The sporadic form of the disease in infants known as posterior basic meningitis is described separately.

The *stage of invasion* may be regarded as a prodromal septicæmia. Onset is abrupt with intense headache, frontal or occipito-frontal, pain in the lumbar region and legs, vomiting, often projectile, shivering, rigors, or

convulsions in the child, pyrexia of 102° to 103° or more, and sometimes delirium. These symptoms may continue and become intensified for a period varying from twenty-four hours to sometimes as long as three or four days. Occasionally there is a remission of severity after the first twenty-four hours, but the symptoms return with increased intensity. During this stage, and before the appearance of meningeal symptoms, petechiæ may be seen upon the back and abdomen, less frequently upon other parts of the body. Coalescence of petechiæ may, in severe cases, result in purpuric blotches. That these petechiæ are caused by septicæmia is evident from the fact that the meningococcus has been recovered from them. Erythematous rashes, scarlatiniform or morbilliform in type, may also appear during this phase. Both types of eruption may make their first appearance when meningitis has become manifest, but they are none the less septicæmic manifestations. Petechiæ occur most constantly in the severe "epidemic" form of the disease; in sporadic cases they are less common. Herpes facialis and labialis vary in their incidence in different epidemics. Owing to instability of the vasomotor system, tâche cérébrale can be produced but is not diagnostic of meningitis.

The meningeal stage is characterised by the continuance and exacerbation of headache which becomes excruciating; pain in the back, especially in the lumbar region, becomes more marked and is often accompanied by hyperæsthesia. Rigidity of the neck is a very early and constant sign, which renders flexion impossible. Photophobia is frequent, and the patient is irritable and resents disturbance for any purpose. Rigidity of the neck is succeeded by retraction of the head, which may become extreme and a position of opisthotonos may be assumed. The abdomen is retracted. The pupils are dilated and the light reflex is sluggish. Usually there is moderately increased rapidity of the pulse, but occasionally bradycardia occurs and the blood pressure is low. The temperature in cerebrospinal fever is most variable, but usually at this stage is maintained round about 103° or 104°. Temperature is influenced largely, no doubt, by coincident septicæmia. Kernig's sign and Brudzinski's neck sign can almost always be elicited. The knee jerks may be brisk or absent, and the plantar response is indefinite; the abdominal reflexes are usually present. The *blood* always shows a leucocytosis of from 20,000 to 30,000.

The *cerebrospinal fluid*, obtained by lumbar or cisternal puncture in children and adults, and occasionally by intraventricular puncture through a lateral angle of the anterior fontanelle in infants, completes and confirms the clinical evidence. Before the onset of true meningeal symptoms, the cerebrospinal fluid, although under pressure, may be clear and capable of reducing Fehling's solution. The puncture fluid obtained in the meningeal stage is always under increased pressure and may spurt from the cannula. It is turbid, and may contain flakes of pus; occasionally it is so thickly purulent as to escape with difficulty from the cannula. The presence of blood is probably always to be ascribed to trauma produced in introducing the lumbar puncture needle into the intrathecal space. Cytological examination of the fluid shows a great increase in the polymorphonuclear leucocytes. Gram-negative diplococci can be seen, both intra-cellular and extra-cellular. The proportion of intra-cellular to extra-cellular organisms has some prognostic value, a preponderance of intra-cellular diplococci being of more favourable import. Cultures made immediately upon blood-

agar, and incubated without delay, will yield colonies of the meningococcus. The protein content is increased and the chlorides diminished. There is no reduction of Fehling's solution. It should be added that these changes are common to any purulent meningitis.

The *course* of the epidemic form varies. Death may occur in a few hours or a few days from onset in the fulminating or hyperacute types, or the patient may recover from the acute phase and die later from some complication or from asthenia. Recrudescences are common; relapses not rare. The usual type of temperature is intermittent, with a tendency to irregularity. This intermittent pyrexia may continue for three weeks or more. The acute phase may end by crisis and recovery or in fatal hyperpyrexia. It must be stressed that these remarks apply to the untreated or imperfectly treated case. With adequate chemotherapy, recovery is the rule and is soon brought about.

Recovery is heralded by the disappearance of all objective and subjective signs of meningitis; the temperature falls, and the mental condition which was previously clouded to a greater or lesser degree becomes normal. When the acute phase is at an end the cerebrospinal fluid no longer escapes under pressure, and is clear. The cell count is normal and diplococci are no longer to be seen; the fluid is sterile on culture and its power to reduce Fehling's solution returns.

Posterior Basic Meningitis.—A. C. Hampson regards this condition as a sequel in infants to a mild attack of acute meningitis which has escaped diagnosis or as one in which the treatment of the acute phase has not been effective. Thick purulent exudate at the base of the brain results in the closure of the foramina of Magendie and Luschka connecting the subarachnoid space with the ventricular system. There is marked head retraction and bulging of the anterior fontanelle. Lumbar puncture frequently results in a dry tap, and cisternal puncture may be necessary. Unless drainage of the cerebrospinal fluid, which is produced in excess, can be re-established, hydrocephalus ensues, and this entails ultimate death or, at best, mental defect with or without blindness of central origin. The effective treatment of cerebrospinal fever with sulphonamides makes the occurrence of hydrocephalus unlikely.

Fulminating Meningococcal Septicæmia.—In this form death may occur before meningeal localisation is clinically evident, and may be caused by the so-called "adrenal" (Waterhouse-Friedrichsen) syndrome. This is characterised by hæmorrhages into the adrenals, and possibly other endocrine glands, purpura, and extremely low blood pressure with consequent peripheral circulatory failure. The prognosis is extremely bad, but drastic measures (*vide infra* Treatment) are occasionally successful.

Chronic Meningococcal Septicæmia.—During the epidemic of cerebrospinal fever which occurred early in the recent war, a number of cases of chronic meningococcal septicæmia were described without meningitis. The onset is sudden with fever, headache, and pains in the joints and muscles. After a few days a skin eruption appears consisting of pink or red macules, papules and nodules which are often tender, but rarely hæmorrhagic, at any rate at the onset. The condition is apt to be misdiagnosed as subacute rheumatism or erythema multiforme. Although the pyrexia may last for weeks, the patient often does not appear to be seriously ill. Blood culture may give a growth of meningococci. The sulphonamides produce

rapid cure ; but if the drug is not given, meningococcal meningitis often supervenes.

Complications.—During the acute phase retention of urine is common. Incontinence of urine and fæces may also occur. Broncho-pneumonia may prove troublesome and fatal. Septic arthritis, the meningococcus being present in the pus, occurs occasionally. The following complications affecting the *nervous system* may occur : hemiplegia, involving the face and limbs ; peripheral paralyses, caused by the involvement of spinal nerve roots in the inflammatory exudate, may make their appearance in the limbs, particularly the lower limbs. Various types of mental abnormality occur during the acute meningeal stage, and disappear when this stage subsides. More serious are the mental states which may develop during convalescence. These vary from peculiarities of behaviour to definite dementia ; impairment of memory is common. In the majority of cases these mental conditions disappear in time, but certain of them remain permanently. Hydrocephalus is now less common, the result of chemotherapy (*vide* p. 573).

Ocular Complications comprise strabismus, ptosis, and nystagmus. Conjunctivitis is common. Keratitis associated with perforating ulcer and hypopyon may occur, and iritis and optic neuritis are also met with.

Aural Complications.—Nerve deafness may occur, and may disappear in convalescence ; often, however, it persists and is an important cause of deaf-mutism in young children. Banks estimates the incidence as 5 per cent., and rather more than half the cases are total, permanent, and bilateral.

Diagnosis.—In the septicæmic stage it may be impossible to distinguish the condition from other acute diseases with a similar form of onset. Such diverse conditions as pneumonia, influenza, hypertoxic scarlet fever, smallpox, typhoid, typhus, relapsing fever, plague, and heatstroke have been confused. The petechial rash has been diagnosed as that of typhus and hæmorrhagic smallpox. In the meningeal stage the diagnosis is confirmed by the examination of the cerebrospinal fluid. Pneumococcal and streptococcal meningitis are clinically indistinguishable, but are usually secondary to a primary focus elsewhere. It is a wise precaution, as advocated by Flexner, to swab the nasopharynx. Meningococci may be found in the nasopharyngeal secretion even if absent from the cerebrospinal fluid at the time of the first puncture.

Treatment.—The sulphonamides are essential and must be given in massive doses at the earliest possible moment, repeated at four-hourly intervals in order to maintain a sufficient concentration of the drug in the blood stream and cerebrospinal fluid. In the former this level should be from 10 to 15 mg. per 100 c.c. and in the latter 5 mg. per 100 c.c. Details regarding the type of sulphonamide, dosage, and route of administration are given in the section on Sulphonamides (*vide* p. 6). Anti-meningococcal serum therapy is obsolete.

Lumbar puncture must be performed at the outset to confirm the diagnosis and should be repeated at intervals to gauge progress. Adequate chemotherapy renders therapeutic lumbar punctures unnecessary. The sulphonamides are very rarely contra-indicated, but if so, systemic penicillin (*vide* p. 8) is an alternative. Intrathecal injection, whether of sulphonamides or penicillin, is dangerous and unnecessary. Special measures are required for the treatment of fulminating septicæmia, especially if associated with the " adrenal " syndrome. These include soluthiazole intravenously

and penicillin intramuscularly in large doses, intravenous glucose-saline, and, if indicated, adrenaline-replacement therapy (cortical extract or desoxycorticosterone acetate), and intravenous plasma (Banks).

Prevention.—Isolation should be maintained for at least two weeks after the onset, or until two negative nasopharyngeal swabbings have been obtained at four-day intervals. Concurrent disinfection of nasal and oral discharges is important. Efficient masks should be worn by attendants. Immediate contacts and carriers of meningococci should be kept under observation until shown to be bacteriologically free. The clearance of carriers is readily effected by the sulphonamides. In the presence of an outbreak, attention to general health and hygiene is important. Particular care must be taken to ensure that proper spacing in sleeping quarters is available. During prevalence of the disease the kissing of children should be avoided, particularly by those who have been in contact with a patient.

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SEPTICÆMIA

The discovery of bacteria in the circulating blood indicates a *bacteriæmia*. This condition probably occurs fairly frequently without producing severe symptoms. Thus streptococci and other organisms have been demonstrated in blood cultures taken soon after minor operations, such as tooth extraction or tonsillectomy. By the term *septicæmia*, however, more is meant than the presence of organisms in the blood. Septicæmia indicates a clinical condition, which usually results from the presence of hæmolytic streptococci or staphylococci in the blood stream. Septicæmia due to either of these organisms is an acute condition, but when the infecting organism is the *Streptococcus viridans* an entirely different clinical picture is produced, which is known as subacute bacterial endocarditis (*vide* p. 394). Septicæmic phases also occur in infections by organisms other than the streptococci and staphylococci. Thus in the early stages of pneumococcal pneumonia, the enteric fevers, and meningococcal meningitis, blood cultures may be positive ; but this is usually only a transient finding.

Streptococcal Septicæmia.—The source of infection is often obvious and of a local nature, such as cellulitis, whitlow, a finger pricked at operation or autopsy, tonsillitis, or uterine infection. In some cases septicæmia may occur without an obvious focus. The development of septicæmia probably depends mainly on the virulence of the infecting organisms and the resistance of the tissues to infection. Thus when the resistance is lowered by the presence of a chronic disorder, for instance Graves' disease, a virulent septicæmia is liable to occur as a terminal event.

The onset of streptococcal septicæmia is abrupt. If there is a local lesion a lymphangitis is often visible, and the patient presents certain clinical symptoms which point to blood-stream infection. The most important and constant of these is the occurrence of rigors ; should these occur in the presence of a septic focus, they almost certainly indicate a septicæmia, and blood culture is likely to be positive. Fever of an irregular type is almost invariable, and, unless successfully treated with chemotherapy, it may persist for weeks or months. Two other important symptoms are progressive anæmia of hypochromic type and troublesome diarrhœa, which fails to react to the ordinary remedies. The tongue is smooth, red,

desquamated, and often sore. The urine generally contains albumin, casts, and sometimes red blood cells. The skin may show erythematous rashes and petechiæ, and the spleen is often slightly enlarged. When metastatic abscesses are formed the condition is often described as *pyæmia* rather than septicæmia. Such abscesses are specially likely to develop in the pericardium, pleura, or joints. It is important to watch carefully for the development of symptoms pointing to formation of pus, as their relief by surgical drainage is essential.

Staphylococcal Septicæmia.—Infections by the *Staphylococcus aureus* are usually primarily in the skin, and this organism is responsible for boils and carbuncles. The degree of general constitutional disturbance may be slight while the inflammatory process remains localised, but if the organisms reach the blood stream, either as a result of lowered tissue resistance or ill-judged surgical measures, a septicæmia may be produced in which metastatic abscesses are striking features. These may be found most commonly in the bones, in the perinephric tissues arising from a staphylococcal abscess of the renal cortex, in the pericardium, lungs, pleura or elsewhere. Not infrequently there may be a latent period of days or weeks between the occurrence of a boil and the development of symptoms pointing to a metastatic staphylococcal lesion, such as a perinephric abscess. Often, indeed, blood culture is negative, but a transient staphylococcal bacteriæmia must be presumed. In every case of prolonged pyrexia without obvious cause the possibility of a staphylococcal abscess must be borne in mind, particularly if there is a polymorphonuclear leucocytosis. Pyrexia may continue for several weeks before tenderness or bulging in the loin points to a perinephric abscess. Symptoms may also be misleading. Localised staphylococcal abscesses in the lungs may cause hæmoptysis and lead to a mistaken diagnosis of pulmonary tuberculosis. Spasm of the psoas due to perinephric infection may simulate disease of the hip joint, or an osteomyelitis, especially in a child, may be misdiagnosed as acute rheumatism.

Usually staphylococcal septicæmia is less acute in onset than is streptococcal septicæmia. The most desperately ill patients sometimes made a complete recovery even before the advent of chemotherapy.

Treatment of Septicæmia.—The risk of generalised infection can be minimised by careful treatment of local inflammatory conditions and particularly by the avoidance of premature surgical drainage. Moreover, especially in staphylococcal infections, such as multiple boils or carbuncles, the likelihood of a septicæmia can be diminished by due attention to the general health of the patient, who should be advised to take a prolonged holiday following septic infections.

The treatment of septicæmia has been revolutionised by chemotherapy, and particularly in the case of staphylococcal septicæmia by penicillin. The efficiency of chemotherapy, however, must not be allowed to lead to the neglect of general measures designed to maintain and improve the resistance and nutrition of the patient. These include good nursing, a large fluid intake, if possible five pints daily, glucose, and an alkaline mixture. Sedatives, including morphia if necessary, may be required for pain and sleeplessness. The patient must be examined frequently to detect localised suppuration, *e.g.*, in a joint. Small blood transfusions, not more than 10 oz. at a time, are sometimes of value, particularly if the patient is anæmic. Hyperpyrexia calls for tepid sponging.

Staphylococcal Septicæmia.—In this disease, penicillin should be given at the earliest possible moment in three-hourly doses of 50,000 or more units (*vide* p. 9). The temperature should settle and the blood culture become negative in three to five days. The drug should, however, be continued for a further five days or longer if there is any evidence of a local lesion. Localised collections of pus should be drained or aspirated and penicillin injected into the abscess cavity.

Streptococcal Septicæmia.—Although the streptococcus is susceptible to both sulphonamides and penicillin, the latter is as a rule preferable. If it is decided to employ sulphanilamide (for dosage, *vide* p. 7), it is essential to give penicillin if the response is not satisfactory within three days. Sulphonamides and penicillin can be given concurrently.

RHEUMATIC FEVER

Rheumatic fever, or as it is often called, acute rheumatism, is a specific disease characterised by fever, arthritis of a well-defined type, and a tendency to involve the heart. It certainly has no connection with the degenerative forms of arthritis known as osteo-arthritis, and its clinical picture and age incidence does not resemble infective or rheumatoid arthritis.

Ætiology.—Rheumatic fever is primarily a disease of temperate climates in the northern hemisphere. It seldom occurs among the well-to-do and its incidence is highest among the poor. Overcrowding and poverty are probably the most important factors. It is essentially a disease of childhood and adolescence, and is almost unknown over the age of thirty, except in persons who have already had a previous attack. There is no evidence that the disease is hereditary.

The cause of rheumatic fever is still unknown. There is considerable evidence that the disease occurs in children who some ten days previously have suffered from tonsillar infections with hæmolytic streptococci. Although there is little bacteriological evidence to prove that rheumatic fever is directly due to streptococcal infection, it is possible that the presence of such an infection may in some way produce a sensitisation, which may eventually manifest itself as the symptom complex recognised as rheumatic fever. It has also been suggested that the disease is due to a virus. Probably several factors are necessary, in which both streptococcal infection and allergy may play a part.

Symptoms.—There is frequently an association between rheumatic fever and chorea. Sometimes chorea may develop in a patient who has previously suffered from rheumatic fever, and in chorea the heart often becomes involved exactly as it is in rheumatic fever (*vide* article on Chorea, p. 615). In most cases rheumatic fever has a gradual onset with vague pains in the limbs, general malaise, and frequently a sore throat. The temperature soon rises, and ranges from 102° to 104° as the disease becomes well established.

Joints.—The most characteristic features about the joints in acute rheumatism are that the pain flits from joint to joint and that the arthritis is always multiple. The disease involves the larger joints, most often the knees, ankles, and wrists. The smaller joints usually escape. Although

the pain may be severe, particularly on movement or pressure, there is often remarkably little to see on examining the affected joint. Frequently nothing abnormal can be detected, but sometimes the skin may be flushed or the joint slightly swollen by an effusion of fluid. The skin never becomes glazed, indurated, or œdematous, as it may with pyæmic joints. In the course of a day or two the joints first affected become free from pain and tenderness, while other joints begin to be involved in a similar manner.

Skin.—In severe rheumatic fever, particularly in adults, sweating is profuse and sometimes there is a diffuse erythema, which has no clinical significance.

Beneath the skin, but not actually in it, there are sometimes multiple discrete lumps about the size of a pea, which have been termed *rheumatic nodules*. Occurring mainly in children, they always indicate a severe infection, usually with cardiac involvement. The commonest sites for their occurrence are around the wrists, elbows, and over the superior occipital protuberances.

Blood.—A moderate hypochromic anæmia is common and the leucocyte count is usually high, about 10,000 to 20,000. The blood sedimentation rate is invariably raised.

Heart.—No infection is more prone to attack the heart than rheumatic fever, and it is this feature which renders the disease so serious. In every case, however mild, there is some degree of myocarditis, as exemplified by the tachycardia which often persists for some time after the temperature has fallen and joint symptoms have disappeared. The first sound at the apex is muffled in character and a soft systolic murmur is very frequently present, perhaps due to dilatation of the mitral ring. In about 50 per cent. of cases there is evidence of a definite endocarditis, which affects most commonly the mitral valve, often both mitral and aortic, and rarely the aortic alone. A systolic murmur, blowing in character, best heard at the apex, and propagated into the axilla, often indicates mitral endocarditis. With involvement of the aortic valve a soft diastolic bruit is heard either over the base of the heart or along the edges of the sternum. In addition, pericarditis may occur, particularly in severe cases or in recurrent attacks. It may be accompanied by left-sided pleurisy. The heart lesions of rheumatic fever are dealt with in more detail in the section on Diseases of the Heart.

Pyrexia.—In children the temperature is seldom above 102°, but in adults it is often higher. Hyperpyrexia, common before treatment with salicylates, is now almost unknown.

Types of Rheumatic Fever.—In children the joint symptoms are usually not prominent; it is quite the exception under ten years of age for any definite swelling of the joints to occur, and the pain is much less than in adults. Often, indeed, there may be no noticeable arthritis at all, and the diagnosis depends on the development of cardiac lesions. These are much more frequent and severe in children than in adults. The mild type of the disease as seen in children is often called subacute rheumatism. The temperature is only slightly raised with vague aching in the joints, considerable impairment of the general health, and some anæmia; such cases may be associated with severe cardiac involvement. In children, abdominal pain, sometimes suggestive of appendicitis, is not uncommon at the onset of rheumatic fever.

Differential Diagnosis.—There is one pitfall in the diagnosis of rheumatic fever which may cost the practitioner his reputation and the patient his life, namely, a mistaken diagnosis of acute rheumatism in a case of osteomyelitis. Attention to the maxim that rheumatic fever should never be diagnosed in a monarticular arthritis will go a long way towards avoiding so disastrous an error. Further, in osteomyelitis the skin over and surrounding the joint has a red, glazed appearance, and often pits on pressure. In addition, a point of acute tenderness can usually be made out over the site of the disease in the bone.

Acute rheumatoid arthritis (*vide* p. 553) may simulate rheumatic fever, but the joints involved usually include the small joints of the hands, the cervical spine, and often the temporo-mandibular joints, all of which are but rarely affected in rheumatic fever. Moreover the pain does not flit from joint to joint, and periarticular thickening and deformity of the affected joints occur early with striking muscular wasting. In addition rheumatoid arthritis, unlike rheumatic fever, is excessively rare in children.

A multiple arthritis may occur in the course of many diseases such as pneumonia, dysentery, scarlet fever, pyæmia, syphilis, gout, and typhoid, or it may follow gonorrhœa.

Failure of the pyrexia and pain to react to adequate treatment with salicylates is strong presumptive evidence that the case is not one of acute rheumatism.

Congenital heart disease may give rise to difficulty in diagnosis, especially if a child with a congenital heart murmur develops an intercurrent infection. There is, however, often a history of the murmur having been present in infancy, whereas rheumatic fever very rarely develops before the age of four years. The electrocardiogram and X-ray are often of value in differentiation of the two conditions.

Treatment.—The main object in the treatment of rheumatic fever is to avoid cardiac complications with their attendant menace of chronic valvular disease. Only too often, in spite of everything, endocarditis develops, but there can be no doubt that absolute rest in bed from the onset, with careful nursing, go far to prevent heart disease. Owing to the profuse sweating the patient should be nursed in blankets rather than sheets, and if the joint pains be severe, immobilisation of the affected joints by sandbags and elevation of the bed-clothes by a cradle are desirable. Local applications to the joints, such as methylsalicylate liniment, may give some relief. Even when the heart is not obviously involved the patient should remain in bed for a minimum of three months, while in cases with obvious cardiac involvement six months may be required.

Salicylates reduce the temperature and abolish the joint pains within a few days. They have, however, little if any effect on the carditis. Sodium salicylate should be given with an equal number of grains of sodium bicarbonate. An average dose is $1\frac{1}{2}$ gr. of salicylate for each year of the child's age. The doses should be given four-hourly for a fortnight and then be halved. Thus a patient aged ten would take 15 gr. of the drug four-hourly, *i.e.*, 90 gr. per diem. The bicarbonate prevents salicylate poisoning, the symptoms of which are tinnitus, vomiting, and sometimes delirium.

The diet is not important, but during the initial period of pyrexia the patient will probably only be willing to take fluids. If the pain is severe enough to prevent sleep, Dover's powder may be necessary. Within forty-

eight hours of adequate treatment with salicylates the joint symptoms subside, but the carditis may remain active for many weeks or months. It is often difficult to assess when the disease has become inactive. Indications of this are a completely normal temperature and pulse-rate, absence of anæmia and leucocytosis, a normal blood sedimentation rate, and an increase in body weight. The persistence of a systolic murmur is no indication of activity.

Prognosis and Prophylaxis.—The immediate mortality of rheumatic fever is relatively low, but it levies a heavy toll in deaths from cardiac failure in later life. Unfortunately it is a disease which tends to recur. The chances of relapse during the year following the first attack are three times as great as in subsequent years. Special care is, therefore, essential during this period. With each recurrence the chances of severe and permanent cardiac damage become increased. If possible the patients should live in the country, and all predisposing causes of further attacks such as under-nutrition, overcrowding, overwork, cold, and chills must be avoided. Unfortunately, at any rate in hospital patients, this is an ideal unattainable in the present state of society and economics.

It is important not to restrict unduly the activity of children who have suffered from rheumatic fever. If there is no evidence of a cardiac lesion they may be allowed to lead a normal life. When valvular disease is present competitive team games should be forbidden, but reasonable exercise which does not produce distress is beneficial, both from the point of view of health and morale.

Tonsillectomy is inadvisable unless there is gross sepsis ; in any case the the operation should not be performed until convalescence is completed.

ERYTHEMA NODOSUM

This condition is not a manifestation of acute rheumatism and does not produce cardiac lesions. It occurs chiefly in children and young adults. Indurated red areas appear chiefly over the shins, rarely on the forearms. These are raised above the surface of the skin and are very tender. Usually circular or oval, they vary in size from a half to two inches in diameter. At first they are red, but later become purple. There is usually little constitutional disturbance, but sometimes there may be fever and vague joint pains.

The ætiology of the condition is not definitely established, but it is probably a cutaneous response to bacterial allergens, which are usually either streptococcal or tuberculous. This is suggested by the fact that patients suffering from erythema nodosum frequently show evidence of chronic infection, such as enlargement of the tracheo-bronchial glands, infected tonsils, and chronic enlargement of the glands in the neck. Many cases give a positive Mantoux test and are tuberculous in origin ; others react to hæmolytic streptococcal endotoxin.

There is no specific treatment, and with rest in bed and local applications of lead lotion the lesions usually clear up within a fortnight. In view of the frequent tuberculous origin of the disease X-ray examination of the chest is essential and should be repeated at intervals.

INFLUENZA

Probably no diagnosis is made so frequently and often with so little justification as that of influenza. The layman, indeed, is very apt to term any severe nasal catarrh or infection of the upper respiratory tract an influenzal attack. How different such cases are from the true epidemics of influenza is well illustrated by the devastating pandemic which occurred in 1918 and 1919. Perhaps the most striking point about the disease is the way in which it occurs in widespread epidemics, independent apparently both of climate and nationality. In 1918 the number of deaths from the disease must have far exceeded the total of those killed in the war. Similar pandemics occurred in 1889 and 1899.

Ætiology.—The brilliant work of Laidlaw and others has shown that influenza, at any rate in some epidemics, is due to infection by a virus. Pfeiffer's bacillus (*Hæmophilus influenzæ*), formerly thought to be the causal organism, is now known to be a secondary invader, as also may be streptococci or pneumococci. The complications of influenza, such as pneumonia, are due to secondary invading organisms. The disease is extremely infectious, as the virus is widely scattered by the patient's cough. An attack produces a relatively short period of immunity, and some people appear to be specially susceptible to infection. In pandemics the disease is usually more severe in young and healthy adults than in infants or the aged.

Symptoms.—The onset is always sudden and the incubation period very short. Any attempt to describe the clinical features is necessarily difficult owing to the wide variations which occur in the disease in different localities and at different times. The cases can, however, be divided roughly into the so-called simple influenza and those with pulmonary involvement. The former type is met with in periods between widespread epidemics, and also includes the great majority of the cases even in pandemic periods. The disease begins with severe headache, aching of the joints, and pyrexia: the fauces are red and injected, but without definite tonsillitis; a hard, hacking cough due to tracheitis develops early, but usually there is little sputum. After a few days of irregular pyrexia, with considerable prostration, the symptoms disappear and a slow convalescence ensues. In some epidemics complications such as acute otitis media, mastoiditis, sinusitis, and rarely meningitis are frequent. Severe post-influenzal mental depression is not uncommon.

In some epidemics gastro-intestinal symptoms are prominent, and such cases are often described as *gastric influenza*. The temperature is rarely above 100° F.; the tongue is furred and the patient suffers from abdominal discomfort, nausea, and vomiting. The bowels are usually constipated. Needless to say, the diagnosis must be made with caution, especially in the absence of an epidemic.

The pneumonic or septicæmic type of influenza presents a very striking picture. Often starting with symptoms similar to those of the simple form of the disease, it rapidly becomes apparent that the illness is of a grave type. The breathing is rapid and shallow, though there is no obvious respiratory distress; cough is frequent and troublesome; the sputum becomes considerable and is frothy and hæmorrhagic. But perhaps the most striking feature is the colour of the patient, which ranges from pink in the

milder cases to a characteristic heliotrope, lilac, or violet hue in those who are desperately ill. The pyrexia is not necessarily high ; in fact, in the more severe cases the patient may die with a subnormal temperature. Although involvement of the lungs is the most obvious feature, streptococci can sometimes be cultivated from the blood, indicating the presence of a true septicæmia. These organisms, however, are probably secondary invaders. The kidneys are affected, as is shown by the presence of albumin and casts. The mind is clear and alert to within a few hours of death, though occasionally delirium and convulsions occur, which are not, however, necessarily indicative of a true meningitis.

The physical signs in the chest are very variable, and are of little value in assessing the severity of the disease. Sometimes nothing is heard except a few scattered râles and rhonchi ; sometimes there may be dullness and bronchial breathing over a considerable area of lung. Often the physical signs vary considerably from day to day. The pulse is usually relatively slow compared with the temperature and respiration rate. Pleural effusions, empyema, or rarely pulmonary abscess may be serious complications or sequelæ.

Prognosis.—In sporadic cases of influenza death hardly ever occurs. In epidemics the death-rate varies with the proportion of pneumonic cases. The most significant point in the prognosis is the colour of the patient ; those with the typical heliotrope tint invariably die very rapidly.

Diagnosis.—In the presence of an epidemic the diagnosis is easy. With sporadic cases influenza should not be diagnosed until other pyrexial illnesses have been excluded.

Treatment.—There is no specific treatment for influenza, but without doubt immediate confinement to bed tends not only to shorten the course of the illness but diminishes the incidence of complications. It also helps to limit the spread of the disease. Symptomatic treatment with aspirin (10 gr.), Dover's powder (10 gr.), and steam inhalations give relief. If cough is troublesome, a linctus containing equal parts of syrup of codeine phosphate and syrup of Virginian prune is often effective in 2-drachm doses.

Influenzal pneumonia is due to invasion by secondary organisms. As these may be sensitive to penicillin or sulphonamides, one or both of these drugs should be tried, though they are certainly of no value in uncomplicated cases of influenza.

Convalescence is often slow even after mild attacks, and several days of rest should be insisted on before the patient returns to work.

GLANDULAR FEVER

Though febrile illnesses associated with glandular enlargement were described many years ago the conception of glandular fever as a definite disease entity has only become firmly established during recent years. Moreover, with the advent of specific laboratory tests it is probable that the malady may prove to be much more common than was supposed.

Ætiology.—Nothing is known of the nature of the disease, though its infectious or contagious character is proved by its occurrence in epidemics, often institutional. Though originally thought to be primarily a disease of young children, it is becoming increasingly clear that glandular fever

is far from uncommon in adults. It may indeed account for many mild "pyrexias of unknown origin."

Clinical Picture.—Glandular fever has been described as of three types: (i) glandular; (ii) anginose; (iii) febrile. Needless to say, these types overlap and the terms are of little value save in emphasising the main presenting symptoms in each case. The glandular type is chiefly seen in children, while the anginose and febrile types are more common in adults. The onset may be abrupt or insidious.

Lymphatic Glands.—The glands in the neck are most often involved, but those elsewhere may also be enlarged. They are usually though not necessarily tender, and movement of the neck is painful owing to the adenitis. The spleen may be slightly enlarged.

Throat.—A slightly sore throat is common in all types, but in that described as anginose there is a membrane over the tonsils sometimes involving also the fauces which closely resembles diphtheria. The condition develops slowly as compared with diphtheria, and is usually preceded by a period of pyrexia.

Rashes.—These occur particularly in the more prolonged febrile types in adults. The rash appears towards the end of the first week and may closely resemble that of typhoid, measles, or rubella. It involves chiefly the trunk and comes out in crops. It occurs only in a minority of cases.

Pyrexia.—The duration of fever is very variable, but in adults it may last for several weeks and precedes glandular enlargement. In children there is often only a few days' fever while the glands are enlarged. The temperature is often high—104° F. or more—in the anginose types.

In addition to the features described above there may be epistaxis, vomiting, diarrhœa, jaundice, cough, and pain in the chest, and rarely a meningitic reaction.

Diagnosis.—The disease is so protean in its manifestations that except in epidemics the diagnosis can seldom be made with certainty except with the aid of the laboratory investigations.

The Blood Picture.—After an initial increase in the neutrophils for a few days, an absolute mononucleosis develops which has given the disease its alternative title of *infectious mononucleosis*. More rarely there may be an initial leucopenia. When the disease is fully developed, the total white count is usually between 10,000 and 20,000 cells with 50 to 80 per cent. of mononuclear cells. These include a few small lymphocytes, but mostly they are large lymphocytes and often atypical lymphocytes which may resemble those seen in lymphatic leukæmia. A relative lymphocytosis may persist for many months after all symptoms have disappeared. Apart from the white cell count there are no abnormal features as regards the blood. The blood sedimentation rate is usually normal except in the anginose type and when high fever is present.

Paul-Bunnell Test.—The blood of patients with glandular fever contains heterophil antibodies which produce agglutination and hæmolysis of sheep's red cells. These antibodies are not present in normal human blood in a titre exceeding 1 in 8. In glandular fever the titre may rise to very high figures, but a titre of 1 in 64 is almost diagnostic. Occasionally the Paul-Bunnell test is not positive for seven to fourteen days after the onset of symptoms. Positive Wassermann and Kahn reactions have also been reported, but these are transient.

Differential Diagnosis.—Sporadic cases of the anginose type may be confused with diphtheria or Vincent's angina, but the clinical features and the blood count should render confusion unlikely. The prolonged febrile types, especially if there is a typhoid type of rash, may lead to a suspicion of enteric fever. The patient, however, is not so obviously ill as might be expected with typhoid, and the laboratory findings will usually differentiate the diseases. In the rare meningitic form of the disease tuberculous meningitis may be suspected. In leukæmia there are usually anæmia and hæmorrhages, while the leucocyte count is likely to be higher than in glandular fever and with more definitely abnormal white cells. In rubella the Paul-Bunnell is always negative as it also is in secondary syphilis.

Prognosis and Treatment.—Complications such as suppuration of glands are extremely rare and complete recovery is almost invariable. Treatment is purely symptomatic. Sulphonamides are of no value.

UNDULANT AND ABORTUS FEVER

Two closely allied organisms, *Brucella melitensis* and *Brucella abortus*, cause in man a prolonged pyrexia with a tendency to remissions and relapses. *B. melitensis* is primarily an infection of goats, *B. abortus* of cattle. Man is infected through drinking the milk. Although there are minor differences in the clinical features of undulant fever (Malta fever) and abortus fever, there is sufficient similarity in the two infections, as seen in man, to warrant their being described together.

Symptoms.—The onset is gradual with pyrexia, sweating, and sometimes rigors. Although the fever may be high, the patient often feels relatively well, and sometimes may even remain ambulant for long periods. The pulse is relatively slow and the patient is clear and alert. Sometimes the spleen is just palpable. In undulant fever joint pains and arthritis may occur, but this complication is rare in abortus fever. The symptoms may last for many months with exacerbations or remissions.

Diagnosis.—The possibility of abortus fever must always be borne in mind in any case of prolonged pyrexia without an obvious cause. Suggestive clinical features are the very profuse sweating, relatively slow pulse, and the fact that the patient is not as ill as might be expected with the prolonged fever. In all cases of continued fever, agglutination tests should be performed. The agglutination titre usually rises to 1 in 1,000 or even higher. The organism can sometimes be obtained by blood culture.

Prophylaxis and Treatment.—Efficient pasteurisation affords complete protection. As many apparently healthy cows may be carriers, raw milk is always potentially dangerous.

The disease tends to spontaneous cure, though relapses may continue for many months. Rest in bed in the earliest stages probably cuts short the duration of the illness. Sulphonamides and penicillin seem to have little if any effect.

SPIROCHÆTOSIS ICTERO-HÆMORRHAGICA

Spirochætosis ictero-hæmorrhagica (Weil's disease) is a febrile jaundice due to infection by a spirochæte, the *leptospira ictero-hæmorrhagica*, which

is excreted in the urine of rats. Presumably the organism penetrates the sodden but intact human skin. The disease occurs in miners, workers in sewers, fish-cleaners, or wherever water is likely to be contaminated by the urine of rats.

Symptoms.—The onset is invariably sudden with high temperature and often a rigor. Headache, vomiting, and severe muscular pains are the main features during this initial febrile stage, but there is often nothing specially characteristic until jaundice develops on the fifth or sixth day. During the pre-icteric stage the diagnosis may be suggested by the occupation, labial herpes, often hæmorrhagic, and conjunctivitis.

The jaundice is deep and the patient appears orange-coloured. Bile is present in the urine, but the fæces are not necessarily clay-coloured. In severe cases there is great prostration and often a tendency to hæmorrhage, producing epistaxis, petechiæ, or even hæmatemesis or melæna. The urine contains albumin, casts, and blood. Usually after a week or two the jaundice gradually disappears and convalescence is established, but a proportion of the patients develop anuria and die from uræmia and exhaustion. The temperature falls within a few days of the development of jaundice, but there is sometimes a secondary rise of temperature about the third week of illness. Probably many mild cases occur in which jaundice is absent. Except in localised epidemics these are likely to be misdiagnosed as influenza.

Diagnosis.—A definite diagnosis can be made by inoculation of the patient's urine into a guinea-pig. The urine does not contain the leptospira until about the tenth day. Agglutination tests are likely to be positive about the sixth day. Blood culture is negative except during the pre-icteric stage.

A polymorphonuclear leucocytosis is found in spirochætosis, in contrast to the normal or low white-cell count in toxic or infective jaundice. Spirochætosis should be thought of as a possibility in all cases where jaundice develops after some days of a severe febrile illness, especially if the patient's occupation is one which involves getting wet in rat-infested surroundings.

Treatment.—The value of the specific anti-serum is doubtful. The spirochæte is sensitive to penicillin *in vitro*, but there is as yet no definite clinical evidence of its effectiveness. The patient should take large amounts of glucose and fluids, and fats should be avoided. Symptomatic treatment is required for the headache and other symptoms.

TETANUS

Ætiology.—The disease is due to infection by the *Tetanus bacillus*, which is usually present in cultivated ground, road dust, and horse manure. The bacillus is anaerobic, and forms spores which are extremely resistant to heating and drying. Infection occurs through contamination of wounds, though these may be so slight that they may escape detection.

Pathology.—The bacilli multiply at the site of inoculation with the production of a most virulent toxin. The latter has a special affinity for the central nervous system ; this it reaches by passing up the motor nerves, possibly through the axis cylinders or in the perineural lymphatics. Once the toxin reaches the central nervous system it appears to form some kind of combination with the nerve tissues and the symptoms of the disease become manifest. Owing to the anaerobic character of the bacillus it is more likely to flourish in deeply punctured wounds than in superficial abrasions.

Tetanus bacilli in a virulent form may often be cultivated from the site of infection long after the disease has become established ; whether such a focus continues to manufacture toxin is not clearly established. It is possible that the tissues of the patient may have already acquired anti-tetanic powers sufficient to neutralise the formation of further toxin, though ineffective in dealing with that formed and conveyed to the nervous system during the earlier stages of the disease.

At autopsy there may be hypostatic pneumonia and occasionally rupture of muscles, particularly the rectus abdominis, owing to the spasms.

Symptoms.—The period which elapses between the infection and the development of symptoms varies from two to twenty days or even longer. The first sign of the disease is usually a stiffness or rigidity of the muscles of mastication or of the neck muscles, which is frequently first noticed when the patient awakes in the morning. The description of a patient with tetanus, written by Hilton Fagge in his textbook of medicine over fifty years ago, cannot be improved upon. After describing the inability to separate the teeth known as *trismus*, he continues : " The toxic spasm increases and spreads to the muscles of the trunk, and to at least the upper parts of the limbs. The patient's aspect is then very remarkable. The face may be described as having an unnaturally aged appearance, the forehead being wrinkled and the features contracted and drawn. The angles of the mouth are wide apart, and the lips are stretched over the closed teeth, so as to produce a fixed smile, which is known as the *risus sardonicus*, and is at once seen not to be indicative of any pleasurable feeling. The alæ nasi are thrown outwards, and the nasolabial furrows are exaggerated. The eyelids are half closed, but the eyes are said to have a staring expression, although their muscles are seldom if ever affected by the cramp. The jaws may be so firmly clenched that not even a paper-knife can be wedged in between the teeth, or perhaps they can still be separated a little way from one another. The body is rigid, and it is almost curved, so that the back forms a deep hollow. This condition is called *opisthotonos*. At the same time the chest is, of course, thrown forwards, and it is more or less fixed in a state of expiration, while the abdomen is flat or sunken. The tension of the affected muscles is obvious to the touch and sight ; this is particularly the case with the recti abdominis, which are often described as feeling ' as hard as boards,' and which in persons who are not too fat stand out in knotty masses through the integuments."

Pain is an early feature of the disease ; the breathing is embarrassed and the voice reduced to a whisper. From time to time reflex spasms with *opisthotonos* occur, which are usually attended by a great increase of pain. These paroxysms may occur spontaneously or be brought on by slight external stimuli, such as a sudden noise or draught of cold air. The mind usually remains perfectly clear. Pyrexia is variable, but sometimes it may be very high. Death may occur early in the disease from respiratory paralysis ; in the more protracted cases, even though the spasms may have ceased, the patient may die of exhaustion, pneumonia, and heart failure.

What is known as " local tetanus " is met with occasionally, especially in those who have received prophylactic serum ; in this, spasms affect only groups of muscles in the neighbourhood of the site of infection.

Symptoms of tetanus may develop when an old wound is reopened. Before any such operation a prophylactic dose of serum (3,000 units) should be given.

Diagnosis.—Strychnine poisoning may simulate tetanus. In this the muscles of the hands are more often involved than in tetanus, and, also, the muscles do not remain rigid between the paroxysms. The trismus of tetanus must be distinguished from that due to local causes about the jaw, such as dental irritation. Occasionally the fear of " lock-jaw " may produce hysterical symptoms, which superficially may resemble tetanus.

In meningitis, although opisthotonos and neck rigidity may be striking, absence of trismus usually makes the diagnosis apparent. Moreover, in tetanus the cerebrospinal fluid is clear unless serum has been given intrathecally.

Prognosis.—The longer the interval between the occurrence of the wound and the first manifestations of the disease, the better the prognosis. Where this is less than eight days the outlook is bad. Even more important from the prognostic point of view is the length of time that elapses between the first symptoms of *trismus* and the onset of reflex spasms. When this is less than forty-eight hours, recovery is improbable. Unfortunately, even with new methods of treatment, there is little improvement in the prognosis of fully developed tetanus.

Prophylaxis and Treatment.—The value of anti-tetanic serum as a prophylactic measure is universally recognised. At least 3,000 units should be injected subcutaneously as early as possible after all wounds, particularly if these have occurred on a road or cultivated ground. Even a graze on the skin or small puncture wounds are potentially dangerous. Further injections should be given at weekly intervals until the wound is completely healed. Failure to give prophylactic serum can only be regarded as criminal negligence.

Active immunisation with tetanus toxoid produces an immunity, the degree and duration of which is doubtful, and as a prophylactic measure it in no way supersedes the prophylactic serum. Two doses of 1 c.c. should be given subcutaneously at an interval of not less than six weeks.

In the treatment of tetanus there are four essentials : (i) an adequate amount of serum given at the earliest possible moment with a view to the neutralisation of further toxin formation ; (ii) sedatives to diminish muscular rigidity and the severity of spasms ; (iii) adequate nutrition ; (4) cleansing and drainage of the wound.

Serum Treatment.—Although it is doubtful whether anti-tetanic serum has any appreciable effect in neutralising toxin which has already reached the nervous system, it is certainly able to neutralise any further toxin which may be formed in the focus of infection. The best method of giving serum is intravenously, and a large dose, certainly not less than 100,000 units and preferably 200,000 units, should be given at once. When large doses of serum are given intravenously it has been shown that a considerable portion of the antitoxin remains in the blood for three weeks or longer and there is therefore no need to give subsequent doses. Serum should not be given intrathecally, as it frequently produces an aseptic meningitis with severe cerebral symptoms. Intramuscular injections may be used as an adjuvant to, but not as a substitute for, intravenous therapy.

Sedatives.—When the spasms are frequent and severe the use of avertin has proved most valuable. It should be given rectally in full doses (0·1 gm. per kilo of body weight). Avertin usually abolishes spasms and rigidity, thereby preventing exhaustion and facilitating feeding.

Feeding.—Death from exhaustion is less probable if the nutrition of the patient can be maintained. Spasms and rigidity involve the expenditure of much muscular energy, and an attempt must be made to give at least 2,000 calories daily, mainly in the form of glucose, milk, or eggs. If necessary a stomach or nasal tube may be used when the patient is under avertin.

Treatment of the Wound.—The wound should not be dealt with until several hours after a large intravenous dose of antitoxin: otherwise there is liable to be a flood of unneutralised toxin into the circulation. If there is any pus it should be given free drainage, and small wounds or abrasions over which scabs have formed should be opened up and cleansed with hydrogen peroxide.

ANTHRAX

Anthrax is primarily a disease of herbivorous animals, but occasionally occurs in man. In England the disease is mainly found among those who work with hides and animal hair, such as tanners and wool-sorters. Infected shaving brushes have accounted for a number of cases.

The anthrax bacillus is about 7 μ in length, and in culture forms heat-resistant spores. Owing to its large size the bacillus is readily detected as a gram-positive rod in smears from lesions due to anthrax.

The most common form of the disease is a local infection of the skin known as a *malignant pustule*, occurring on exposed parts such as the face, neck, and arms, in those who handle infected material. The first symptom is itching, and in the course of a few days the lesion presents a characteristic appearance. In the centre there is a black slough or eschar due to effused blood; surrounding this is a ring of minute vesicles, and the whole lesion is encircled by a markedly indurated area; the neighbouring glands are swollen but do not suppurate. A striking feature is the absence of pain, as compared with a lesion of similar size due to pyogenic organisms. Often the patient feels quite fit for some days, but later fever and collapse indicate a septicæmia and the prognosis is extremely bad.

Diagnosis of Anthrax.—This is readily made on bacteriological examination. The occupation of the patient and the absence of pain in the local lesion are extremely suggestive, even when the pustule is not characteristic.

Treatment of Malignant Pustule.—On no account should the local lesion be dealt with surgically. Systemic treatment should be instituted at the earliest possible moment, using Sclavo's anti-anthrax serum (repeated intravenous doses of 100 c.c.), neoarsphenamine (0·6 to 0·9 gm.), sulphonamides, *e.g.*, sulphadiazine and penicillin, either singly or in combination.

Pulmonary Form of Anthrax.—This occurs as the result of inhalation of infected material and is known as wool-sorter's disease. The symptoms are indefinite, and consist of a feeling of constriction in the chest, with cough and sputum. The diagnosis is made by the discovery of the anthrax bacillus in the sputum. Death is invariable.

GLANDERS

Glanders is a disease of horses, and is extremely rare in man. The causal organism is *Pfeifferella mallei.*

Human glanders occurs in two forms, acute and chronic. In *acute glanders* the onset is sudden, with fever, malaise, headache, vomiting, and pain in the joints. These general symptoms are rapidly followed by nodular subcutaneous enlargements, known as farcy buds, which quickly ulcerate ; the general picture is one of pyæmia. The disease in the acute form is invariably fatal.

In *chronic glanders* localised nodular enlargements appear on the skin, which ulcerate to form chronic ulcers with indurated edges. The disease may persist in a chronic form for many years, but in some cases an exacerbation of symptoms occurs, resulting in death from acute glanders. In chronic glanders, abscesses must be opened, and, when possible, the cutaneous lesions excised.

ACTINOMYCOSIS

Both local and general infections are sometimes produced in man by organisms of the fungus group, which are known as the mycoses. None is common except actinomycosis, which is caused by the *Streptothrix actinomyces*.

This disease occurs frequently in cattle, and it was formerly maintained that the streptothrix gained access to man through small abrasions around the lips or gums by direct inoculation from straws or grasses held in the mouth. More recently, however, the organism, which in man is anaerobic, has been shown to exist not uncommonly as a saprophyte in the mouth, particularly in carious teeth.

The organism, as seen in pus from an actinomycotic lesion, consists of a mass just visible to the naked eye as a small yellow granule, usually described as a " sulphur granule," the centre of which is formed by a mass of branching filaments with an outer layer of club-shaped bodies. The filaments are gram-positive, but the clubs can be demonstrated only with difficulty.

The disease varies in its clinical manifestations according to the part of the body affected.

1. *The Jaw and Surrounding Structures.*—This is by far the commonest site for infection in man, and probably accounts for well over half the cases encountered. The disease often starts with an injury such as an extraction of a tooth or a fracture of the jaw. In a fully developed case the affected area is indurated with numerous inflammatory nodules, some of which break down and form abscesses, discharging pus which may show typical sulphur granules. The disease tends to spread, often with marked cicatrisation of the older parts of the lesion, and may extend down into the neck or upwards over the maxilla. Secondary infection with pyogenic organisms occurs frequently.

2. *Intestinal Type.*—Infection takes place presumably as a result of swallowing the streptothrix, which tends to lodge most commonly in the appendix, cæcum, or ascending colon. It may produce a close simulation of acute appendicitis, for which the appendix may be removed, and only recurrence of symptoms makes the diagnosis manifest. Sometimes the infection is more chronic and leads to the formation of a slowly growing mass in the right iliac fossa, which consists of adhesions and granulomatous material. Eventually the process involves the abdominal wall with the formation of fistulæ, through which pus and sometimes fæces are discharged.

In the intestinal type of case the infection may reach the liver, which becomes the seat of multiple abscesses with considerable fibrosis. This gives a most striking appearance at autopsy, the liver resembling somewhat a sponge or honeycomb, the interstices of which are filled with pus.

3. *Lung.*—The infection may sometimes reach the lungs by direct spread from the neck into the mediastinum, but most of the cases in which the lung is involved appear to be primary, as the result of inhalation of the organism. Clinically, the cases closely resemble chronic pulmonary tuberculosis with cough, fever, and hæmoptysis. As in phthisis, there may be cavity formation, but, unlike phthisis, sinuses, usually multiple, form in the chest wall.

In severe cases a condition of pyæmia may be established by invasion of the blood vessels ; metastatic abscesses containing the streptothrix form in any part of the body, such as the brain, muscles, or bones.

Course and Prognosis.—The disease is extremely chronic and may last for many years. The pulmonary and intestinal types are usually fatal, but when infection is confined to the jaw and neck there is often complete recovery. Severe secondary infection is an unfavourable feature.

Diagnosis.—In any condition around the jaw, in the chest or abdomen, which is associated with the formation of multiple and persistent sinuses, actinomycosis should be suspected. Sulphur granules in the pus are frequently not seen.

Treatment.—Abscesses and infected areas should be curetted and drained. Iodine appears to control the disease in some cases, and may be given as potassium iodide in very large doses, up to 180 to 360 gr. a day, or as a 10 per cent. solution of iodine ; 4 to 30 minims are given thrice daily in milk. When the disease is localised in one area such as the jaw or the neck, deep X-ray therapy has produced great improvement. Good results have also been reported with sulphonamides and massive doses of penicillin.

PSITTACOSIS

In 1930 outbreaks in England and elsewhere brought this disease into prominence. The infection is primarily one of parrots, but it is highly infectious to man. It is doubtful whether a patient with the disease can infect other human beings. The causal organism is a filterable virus.

After an incubation period of some ten days the patient becomes acutely ill with high fever and severe headaches. The condition soon comes to resemble that of the typhoid state. Pulmonary symptoms are often prominent, and signs of patchy consolidation may appear. Sometimes there is an eruption of rose spots rather resembling those of typhoid fever. After two to three weeks the temperature falls rather abruptly and convalescence is slow.

The diagnosis rests on the history of contact with a sick parrot and the development of an illness resembling typhoid or broncho-pneumonia. Negative bacteriological findings as regards other diseases help to confirm the diagnosis.

Penicillin may prove of value but there is no specific treatment. The mortality is usually about 20 per cent. but varies considerably in different outbreaks.

J. J. Conybeare.

TUBERCULOSIS

PATHOLOGY

TUBERCULOSIS has been recognised from early times. Villemin proved it to be a transmissible disease in 1865, and Robert Koch isolated the bacillus in 1882.

The Tubercle Bacillus.—Tubercle bacilli belong to a class of organisms which stain with basic dyes and which do not easily lose their stain when treated with acids and alcohol—a property which permits this class to be distinguished from other organisms when films or slides containing infected material are stained by the Ziehl-Neelsen method. Several apparently stable types of tubercle bacilli have been isolated and classified according to their pathogenicity. Of these, only the human and bovine types are known to cause tuberculosis in man, although related acid-fast saprophytes occasionally appear in the sputum in cases of bronchiectasis and may thus cause difficulty in diagnosis.

The human tubercle bacillus is a slender rod, commonly slightly curved, and tends to occur in small groups in infected sputum. It is about 5 μ in length. Bovine tubercle bacilli are slightly shorter and thicker. Non-acid-fast granules derived from tubercle bacilli exist, and may be demonstrated in sections of colonies of bacilli on artificial media, and also in healing lesions in human tissues. A controversy exists as to whether or not these granules are capable of giving rise to the organism again, and as to whether a life-cycle of different forms of the bacillus really occurs. The organism is exceptional in many respects; thus fission is relatively infrequent, and its respiration is independent of changes in pH between the wide limits of 1·5 and 12. It is strictly aerobic, because it lacks the ability to induce glycolysis anaerobically. The respiration of cultures of the organism is proportional to the oxygen tension of the environment. This dependence of the organism upon oxygen is a fundamental factor in the pathology of the disease.

Chemical analysis of tubercle bacilli has led to the isolation of constituent carbohydrates, lipoids, fats, and proteins. The lipoid fraction is of particular importance because it varies sufficiently in kind and in concentration in the different types of tubercle bacilli, and in related saprophytic organisms, to permit identification by appropriate analysis; and also because it shares with the protein component of the organism the ability, on injection, of producing the specific tissue reaction—that is, the formation of tubercles—in both normal and previously infected animals.

Tissue Reactions.—Infection by tubercle bacilli may produce various inflammatory tissue reactions. Of these necrosis, exudation, and local cellular proliferation tend to take place early, though in any order or combination. They are in no way specific to the tissue in which they occur. Necrosis and the exudation of fluid, fibrin, leucocytes, and mononuclear cells are essentially similar processes in this, as in every inflammatory reaction. Local cellular proliferation includes the infiltration of the area concerned with macrophages and the formation of epithelioid cells, giant cells, and tubercles. In the lung

the macrophages are typified by "alveolar phagocytes" whose origin is debated. The giant cells which have their nuclei arranged peripherally differ in this respect from those produced, for example, by the irritation of foreign bodies. Occasionally and characteristically these three reactions are together concerned in the formation of tubercles, which consist of epithelioid cells, lymphocytes, and reticulum, varying in quantity and arrangement but often concentrically placed about a core containing necrotic debris and one or more giant cells. Macroscopic tubercles are made up of aggregations of many microscopic tubercles such as the above, and appear as greyish-white translucent small nodules.

Subsequent tissue reactions consist of caseation, liquefaction, fibrosis, calcification, and occasionally ossification. Caseation is typical of tuberculous inflammation. It is preceded by fatty degeneration and necrosis of the tissue cells, and consists in the transformation of such tissue into a somewhat translucent uniform conglomerate. Since considerable areas of lung may be involved quite suddenly, and since the process occurs at a time usually relatively distant from the moment of infection, it has been assumed that a change in the allergy of the patient is an important causal factor. Liquefaction of a caseous area is accompanied by a rapid and considerable increase in the number of adjacent tubercle bacilli, and also by an active local vascular hyperæmia. It seems possible that liquefaction, therefore, is a hypersensitive reaction to the presence of rapidly multiplying bacilli. Following the absorption of the liquid contents of such an area, or their excretion into the bronchial tree, if one or more bronchi be eroded a cavity results. Persistent ventilation of the walls of the cavity gives rise to the aerobic conditions favourable for the growth of tubercle bacilli, while satellite foci may at any time develop if aspiration through the bronchi to adjacent and distant parts of the lungs occurs.

Fibrosis, calcification, and ossification are tissue reactions associated with healing, though the nature of the stimuli which determine their occurrence is unknown. Though varying amounts of fibrous tissue reaction are to be found in most forms of tuberculosis in the lungs and elsewhere, a special example (fibroid phthisis) of the adult pulmonary type of the disease is noteworthy in that the indurative process is pronounced from an early stage, and so continues, with proliferation of fibrous tissue around vessels and bronchi. More or less gross contraction of the lung involved occurs, together with atelectasis, secondary bronchiectatic changes, and compensatory emphysema. The pleura, too, is often grossly thickened in such cases, and the heart and trachea displaced.

Calcification, which is dystrophic, occurs in necrotic and caseous foci, and is found most commonly in tuberculous glands, in primary complexes (Ghon's foci), and in early hæmatogenous secondary lesions as they slowly heal. In these lesions, too, bone may develop, though usually only after many years.

It must be emphasised that within calcified or ossified foci, or foci encapsulated with fibrous tissue, tubercle bacilli may remain alive for many years, and that these healing reactions are essentially reversible processes. It is possible that an alteration in allergy may determine such a reversal, and that under these conditions the foci may again become active and form the starting point for progressive phthisis.

Cases of the common adult form of pulmonary tuberculosis usually show fluctuations of activity of the disease in which these different tissue reactions

variously dominate the picture from time to time. In perhaps a majority of such cases productive reactions—*e.g.*, cell proliferation and fibrous tissue formation—predominate, but are occasionally but remorselessly interrupted by exudative advances, caseation, and liquefaction. The primary focus, and tuberculous lobar and broncho-pneumonia, are examples of lesions in which exudative changes are outstanding ; while miliary tuberculosis—the result of hæmatogenous dissemination of the disease, with its multiple discrete lesions, on the whole of uniform appearance—may show mainly exudative or mainly productive tissue reactions and so give rise to variations in the chronicity of the disease. The commoner, less extensive multiple hæmatogenous lesions, which usually appear soon after primary infection and are distributed towards the apices of the lungs, as a rule are productive in character and tend to calcify (Simon's foci). Isolated large hæmatogenous foci (Assmann's foci) often become caseous, and have a variable subsequent fate.

Blood-vessels, veins, but less commonly arteries, are attacked by tuberculosis. The typical lesion is the intimal tubercle, which differs in no essential of structure from the tubercle described above. The breakdown of such a tubercle may lead to the discharge of tubercle bacilli into the blood-stream, and so to the production of isolated or multiple hæmatogenous lesions, or to generalised miliary tuberculosis. Tuberculosis of the wall of a vessel, especially if supporting structures have been lost as in a pulmonary cavity, may lead to aneurysm formation (Rasmussen's aneurysm). Tuberculous endarteritis is occasionally encountered. Lymphatic vessels, apart from the important part they play in spreading primary infection from an involved organ to the regional lymphatic glands where caseation is common, and thence possibly to the entire lymphatic system of the body or the blood stream, are themselves not infrequently involved. The reaction in rare instances seems mainly to be productive and caseation does not occur, the vessel and adducent glands becoming filled with proliferating cells of the endothelioid type, and lymphatic stasis results. When such a lesion becomes widespread throughout the lungs, the clinical and radiological appearances may resemble those of chronic (hæmatogenous) miliary tuberculosis.

Bronchi and bronchioles are not infrequently eroded by adjacent tuberculous lesions and so become choked with cellular and necrotic debris. Furthermore, tuberculosis, directly or by the blood stream, may give rise to granulomatous bronchitis in which the lumen of the bronchus involved becomes progressively occluded by tuberculous granulation tissue and the stricture-producing consequences of fibrous tissue reaction. This process may extend to the trachea. Bronchial obstruction in this disease may also arise as a result of kinking resulting from the anatomical changes produced by, for example, pneumothorax, or even extensive disease ; as a result of viscid sputum or blood ; and especially in children, by the compression of bronchi by enlarged mediastinal glands. Since bronchial obstruction from all these causes is common, it follows that many different types of tuberculosis of the lungs are frequently and extensively complicated by pulmonary atelectasis, and ultimately by bronchiectasis.

Tuberculosis of mucous surfaces throughout the body gives rise to the same tissue reactions. Granulation tissue, however, tends to be abundant, while caseation and liquefaction lead to ulcer formation. On serous surfaces, such as the pleura, the inflammation may remain dry and the fibrous tissue reaction result in adhesions. Commonly, however, there occurs an

outpouring of clear effusion and cells in the exudative phase. In bone, suppuration is frequent, and may lead to the production of cold abscesses.

Allergy and Immunity.—The tissue reactions to infection by tubercle bacilli are modified by the allergy and immunity of the individual infected. Thus, at the site of reinfection the tissue reaction is intensified and accelerated, as compared with the tissue reaction around a primary infection. Moreover, this hypersensitive reaction in reinfected tissues is more rapidly followed by local disappearance of the bacilli and healing of the lesion. From this observation it was at first deduced that increased tissue activity was responsible for the production of antibodies, and that in fact immunity and allergy in tuberculosis were mutually dependent phenomena. Since caseation and liquefaction were found to occur in association with relatively high degrees of allergy, and since both were harmful to the individual infected, an attitude of despair grew up in regard to immunological therapy—an attitude which was confirmed frequently by disastrous results in practice. Allergy and immunity have since been dissociated experimentally, and it has been shown that the latter can be independently enhanced. In man immunity probably develops with recovery from primary infection, but tends in the course of years to fade ; allergy similarly acquired may wane or, especially in adolescence, may again increase.

A comparison of the subsequent morbidity from pulmonary tuberculosis in groups of uninfected and previously infected young white adults exposed to the same risk of infection would suggest that a considerable acquired immunity may be developed. Furthermore, the immunity of the uninfected individual has been successfully increased by the use of B.C.G. (*vide* p. 98). The ability to develop acquired immunity is probably inherited. Variation in this ability would account for differences in familial and racial response to infection.

Tuberculin Reactions.—Tuberculin reactions have a limited diagnostic value in individual cases, and they may also be used, for example, to survey the incidence of tuberculosis in a population. The reaction is specific, and indicates that allergy to tuberculin has developed as a result of past or present infection. Though the intensity of the reaction is some measure of the degree of allergy, it is not necessarily indicative of the activity of the disease ; moreover, many acute infections such as pyelitis, or measles, or even tuberculosis itself (miliary tuberculosis or extensive phthisis), may diminish tuberculin sensitivity. Finally, after a tuberculous lesion has healed, allergy tends slowly to decrease if reinfection does not occur. The reaction can most conveniently be observed in the skin, and three tests—the von Pirquet (cutaneous), the Moro or patch test (percutaneous), and the Mantoux test (intracutaneous)—are available. The last is performed as follows : The skin on the flexor aspect of the forearm is cleaned with ether, and 0·1 c.c. of a 1 in 10,000 dilution of tuberculin (*i.e.*, 0·01 mg. tuberculin) is injected intracutaneously. The skin is inspected from forty-eight to seventy-two hours later, and a disc of induration more than 8 mm. in diameter around the site of injection is regarded as a positive reaction. If the reaction is negative or doubtful it may be repeated, using a 1 in 1,000 (0·1 mg. tuberculin), or later a 1 in 100 (1 mg. tuberculin) dilution of tuberculin, until an undoubted positive reaction or the last dilution has been attained. Subject to the above-mentioned limitations a negative reaction is strong evidence that infection by tubercle bacilli has not occurred.

Pathogenesis of Tuberculosis

Bovine tubercle bacilli, ingested in infected milk, cause a significant but small proportion of all cases of human tuberculosis. In this country, where bovine tuberculosis is relatively prevalent, between 3,000 and 4,000 cases are found yearly, and the organism causes between 1,000 and 2,000 annual deaths. The patients are mostly young children and their illness is usually recognised at or soon after primary infection, manifesting itself as glandular or disseminated tuberculosis. Less than 1 per cent. of cases of pulmonary tuberculosis arise from this source. Preventive measures, furthermore, may ultimately eliminate this type of the disease, for by 1938 bovine tuberculosis was entirely eradicated in Norway, and it had become a great rarity in certain states in the U.S.A.—as a result of strict preventive measures.

Patients with phthisis, who spray tubercle bacilli into the air on coughing or talking, are the source of the great majority of cases of tuberculosis. Thus in Germany (where bovine tuberculosis is common) more than 90 per cent. of all primary infections occur in the lungs. Infected urine, fæces, or sinus discharges are by comparison of negligible importance.

Tuberculous infection, sooner or later, develops in practically every individual in European and U.S.A. communities; indeed, the incidence of infection approaches 100 per cent. in all classes at the age of forty, although below this age it is higher in every age group among the poorer than in the middle or upper classes. Primary tuberculous infection is now to a less extent predominantly associated with childhood than was the case at the beginning of this century, and many persons reach adolescence or young adult life before becoming infected.

In the vast majority of individuals the infection is overcome, and the various types of progressive tuberculosis do not develop; moreover, the mortality rates caused by the disease have in most civilised countries fallen very considerably in the last two generations. None the less, the disease continues to be one of the worst scourges of humanity. In England and Wales, for example, about a quarter of a million known cases of active tuberculosis were living, and 25,872 deaths occurred from all forms of tuberculosis in the year prior to mid-1939, of which numbers more than four-fifths were examples of respiratory tuberculosis. The war of 1914-18 was accompanied by a rise in the mortality from tuberculosis, and it is significant that to mid-1940 and mid-1941 the corresponding death rates were 27,372 and 28,742—increases respectively of 6 and 11 per cent. above the pre-war level. The mortality has since again decreased.

Our understanding of the factors which determine the development of progressive tuberculosis is incomplete. It is unknown, for example, if natural fluctuations in virulence of the organism occur. In animal experiments the severity of induced tuberculosis is, within wide limits, directly proportional to the size of the infecting dose. In man, however, Chaussé and Lange have shown that the architecture of the bronchial and bronchiolar system is such that only particles of 10 μ or less in diameter can reach the alveoli where infection takes place. Such particles could only contain one or two tubercle bacilli. Since it is known that a tubercle bacillus can give rise to tuberculosis, and that the primary focus is single in almost every case, it would seem probable that for this, the common natural mode of infection in man, the

size of the infecting dose is immaterial, though, of course, the likelihood of infection would probably depend on the frequency of exposure.

Whether reinfection occurs or not is uncertain. Thus pathological evidence suggests that reactivation of previously quiescent foci would account for the bulk of adult tuberculosis. On the other hand, the high incidence of tuberculosis among doctors and nurses, and members of enclosed communities such as nuns or sailors, in all of which instances the chance of reinfection is high, would suggest that exogenous reinfection is common, and leads to progressive disease.

The resistance of the individual to tuberculosis is probably modified by a variety of factors. The twin and family study of Kallmann and Reisner has shown that genetic constitution is a major factor determining not only the likelihood of developing the disease, but also and even more decisively influencing the resistance of the individual to established disease. The negro who fails relatively to develop acquired immunity frequently dies of primary and early post-primary tuberculosis. In most white races with generations of exposure to tuberculous infection the factor of selection has produced a high proportion of those who develop a considerable acquired immunity, and though adult type tuberculosis may be developed the mortality is less and the type of tuberculosis different. Adult type tuberculosis is linked frequently with diabetes mellitus, silicosis, and schizophrenia; it is relatively rare, however, for active pulmonary tuberculosis to be associated concurrently with any other infectious disease. The added burden, and possibly the biochemical changes, associated with pregnancy and its sequelæ not infrequently are accompanied by the development or the exacerbation of pulmonary tuberculosis. The long-recognised association of the disease with poverty, and the rise in the mortality which occurred in the last two wars, would suggest that physical and psychological strain, poor living and working conditions, the increased employment of women, and inadequate diet are significant ætiological factors. That the last is particularly important would seem to follow from the fact that, after a temporary fall, an increase in the mortality of the disease coincided in Germany with the period of inflation in 1922 and 1923. The part played by such factors as leisure, fresh air, light, and personal hygiene is difficult to estimate, since they are largely determined by the standard of life of the individual, which—as we have shown—in turn brings into operation other and probably more important consequences.

Primary Tuberculous Infection

The primary infection, as compared with other tuberculous lesions, presents unique features. Thus the corresponding lymphatic gland and its adducent lymphatics are invariably and rapidly involved whatever the site of the lesion; moreover, this feature and the type of tissue reactions are independent of the age of the infected individual. In the lung the lesion takes the form of an area of broncho-pneumonia, variable in size but usually small and subpleural in position. The local reaction is commonly exudative without typical tubercle formation—showing, however, a marked tendency to necrosis, caseation, and ultimately calcification. Bony tissue may develop in the focus after many years. The same sequence of reactions takes place in the regional lymph gland, and, since abundant interglandular lymphatics are present at the hilum of the lung, many of these glands and those adjacent to the trachea

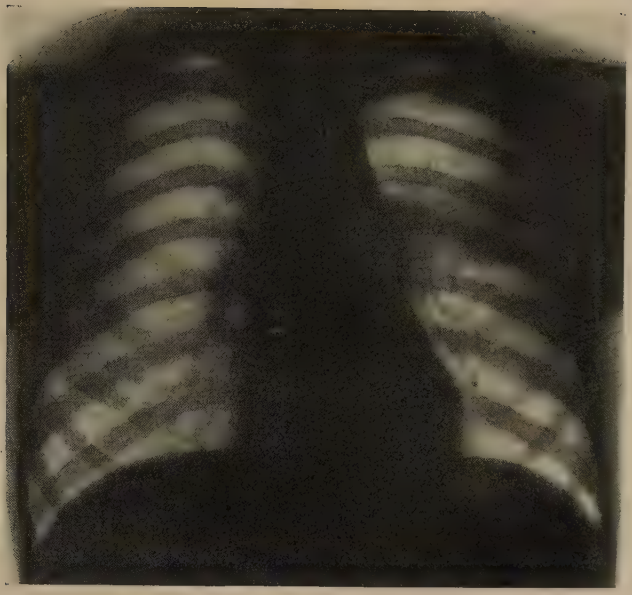

PLATE 1

A large recent primary focus in the left upper lobe associated with hilar lymphadenitis.

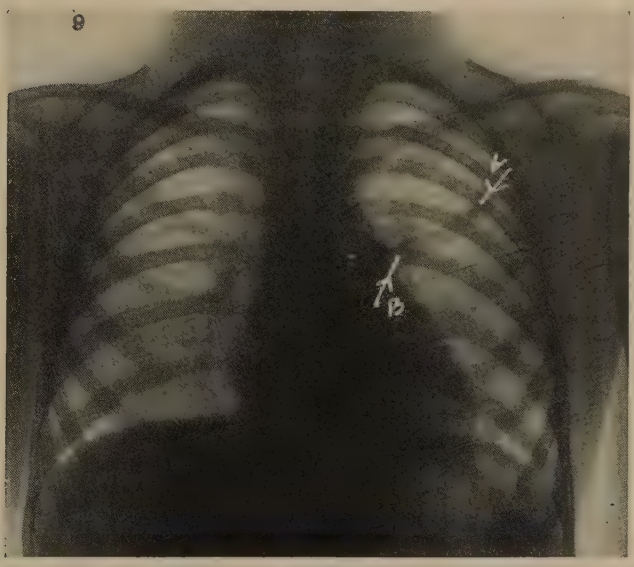

PLATE 2

A healing primary (Ghon's) focus of tuberculosis (A) in the left lung with involvement of the hilar gland (B). Both lesions show early calcification.

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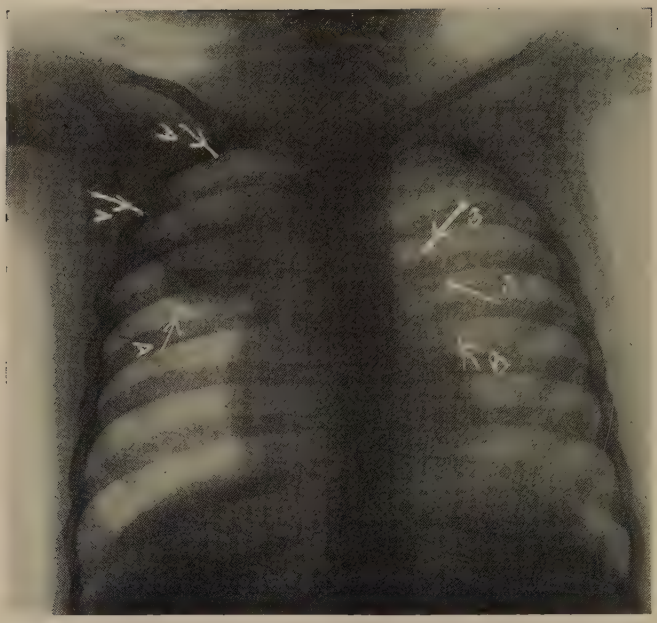

PLATE 3

Epituberculosis, showing a homogeneous opacity involving the right upper lobe (A), and enlargement of the mediastinal glands (B). Atelectasis of the right upper and compensatory emphysema of the right middle and lower lobes are present.

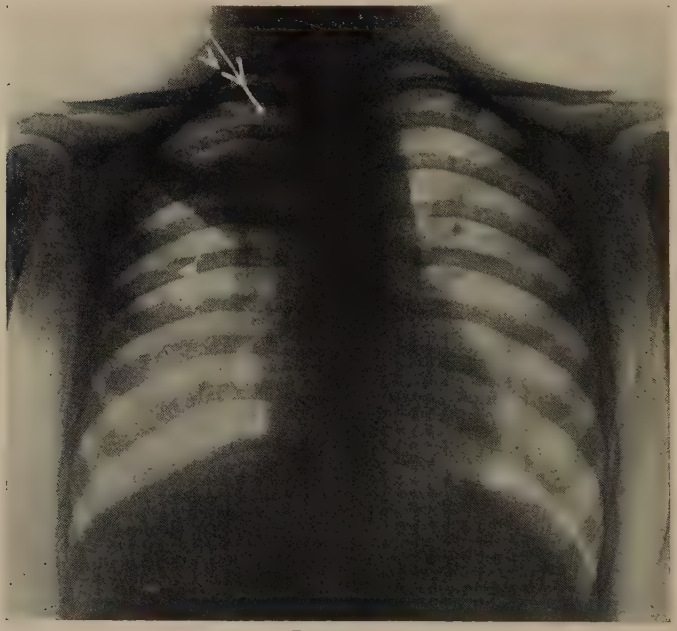

PLATE 4

Epituberculosis. The same case four months later. The opacity (A) in the right upper lobe has decreased in size, and the mediastinal glands are much smaller. Some atelectasis of the right upper lobe is still persistent.

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may be involved from a single pulmonary focus. The glandular component of the primary complex tends to be very large in children; in adults the enlargement, though it occurs, is less apparent. Exactly comparable changes occur when the bacilli first gain entry to the body via the intestine, or in the rare congenital cases via the liver. The intestinal focus as a rule heals completely and may leave no trace of its presence save the diseased glandular component of the complex. Primary foci in skin, tonsils, eye, or middle ear are exceptional. In young adults more often than in children liquefaction of a primary focus in the lung may take place, and give rise to a cavity, from which bronchogenous dissemination of tuberculosis may result. Sometimes ulceration of a bronchus by the glandular component of the complex may lead to this type of extension of the disease. Hæmatogenous dissemination, which tends to occur relatively early, is a fairly common consequence of primary infection, and here also the infected gland is probably more frequently the source than is the pulmonary focus.

Probably the majority of all primary infections cause so little constitutional or local disturbance that they pass entirely unnoticed. None the less pyrexia, which may be severe and of days or weeks duration, may occur and may be accompanied by malaise, cough, and occasionally pleuritic pain. The illness is commonly diagnosed as influenza. Intestinal primary infection is also usually symptomless, though infrequently constitutional disturbance, pyrexia, constipation or diarrhœa, occasionally vomiting in children, and pain in the right lower quadrant of the abdomen may occur. In the chest physical signs are usually not abnormal, though rarely a transient pleural rub, or a few localised râles, may be heard; while in the abdomen local tenderness, muscle spasm, and palpable glandular enlargement may be found. Primary tuberculous infection is not infrequently followed by erythema nodosum, or by pleurisy with effusion. These lesions develop when hypersensitivity to tuberculin is great—often within a year of infection.

The tuberculin reaction may be the only means of diagnosis of primary infection.

The proportion of primary pulmonary tuberculous foci which are demonstrable radiologically is unknown. Undoubtedly the commonest radiological abnormality associated with the lesion is enlargement of the mediastinal glands, though considerable radiological experience is needed to dissociate pathological hilar glandular enlargement from the normal variations of blood-vessel shadows ordinarily aggregated in this region. The appearance with time of calcification in these glands will confirm the diagnosis. The pulmonary component of the primary complex when visible commonly takes the form of an isolated, often rounded, homogeneous shadow (*vide* Plates 1 and 2). Quite frequently, too, the focus is seen to consist of a group of small flecks. The size of such foci, when uncomplicated, varies considerably but rarely exceeds an inch in diameter. Simultaneous hilar adenitis can usually be demonstrated. It is noteworthy that radiologically primary lesions are seen most often in the right lower and middle lung fields. As a rule the peripheral focus slowly calcifies, though occasionally—and then usually shortly after its appearance—it may excavate and leave a thin-walled cavity. In such cases tubercle bacilli may sometimes be demonstrable in the sputum or gastric residue; frequently, however, these investigations are negative.

Epituberculosis.—Commonly associated with the development of the primary complex in the lungs of infants and children is the complication which has been called Epituberculosis. Various hypotheses as to its pathological basis exist. Thus Rossle suggested that the lesion was constituted of the primary complex together with pulmonary atelectasis secondary to bronchial obstruction by enlarged caseous glands. On histological grounds the appearances have been ascribed to a non-caseating tuberculous pneumonia ; to an allergic tissue reaction dependent upon the aspiration of dead tubercle bacilli, or to the diffusion of tuberculo-toxins following the erosion of a bronchus by the primary focus. On clinical and radiological grounds atelectasis would seem to be a probable component of the lesion. In a series of cases of epituberculosis in which bronchoscopy and measurement of the intrapleural pressure on the affected side were undertaken, the author found that bronchial occlusion by compression or, less commonly, by caseous debris could frequently be seen, while the intrapleural pressure was in every case unduly negative—a finding characteristic of atelectasis. Whichever of these hypotheses is correct, it is certain that the patient is allergic to tuberculin and presumably develops immunity, for the skin reactions are positive, and the infection is almost invariably overcome. Not infrequently tubercle bacilli can be demonstrated in the sputum or gastric residue, directly or after culture.

The symptomatology, like that of primary infection, may be inconspicuous, though more often malaise, cough, pleuritic pain and irregular pyrexia of some duration are noticeable. Abnormal signs may be absent, though when extensive areas of lung are involved impairment of movement, percussion note, and air entry may be found, together usually with some mediastinal displacement toward the affected side and sometimes bronchial breathing and râles over the area concerned. The radiological appearances (*vide* Plates 3 and 4) consist of a diffuse and homogeneous opacity extending out toward the periphery of the lung from the hilum, and it is sometimes possible to distinguish within this area the darker opacity of the peripheral caseous lung focus. The lesion is very frequently bounded by an interlobar fissure on one side, commonly that between the upper and middle lobes on the right. Mediastinal displacement toward the lesion and compensatory emphysema are frequently apparent, as are enlarged hilar glands. With healing, the opacity shrinks towards the hilum ; the focus is exposed and may by now be showing calcification, as may the hilar glands ; while ultimately complete return to normality, a calcified complex, or a residual fibrosis with localised bronchiectasis may result. It is probable that a considerable proportion of cases of bronchiectasis—especially apical bronchiectasis—originate in this way.

Treatment of Primary Tuberculous Infection.—The increased examination of contacts to cases of adult type pulmonary tuberculosis, and the development of fluorographic surveys of large sections of the population, have recently revealed, and will continue to reveal, a considerable number of cases of primary tuberculosis in the active stage. In the past the bulk of these cases have been untreated, and the vast majority have satisfactorily overcome the infection, so that it would seem probably to be unsound to advocate institutional treatment for more than a selected proportion. Certainly, where home conditions are satisfactory, when the source of infection can be segregated, and when continued medical (including radiological) examination

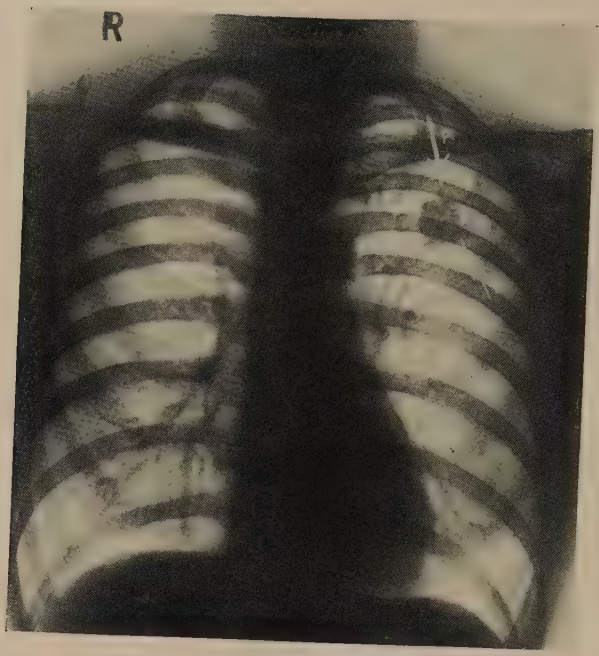

PLATE 5

A secondary (Assmann's) focus of tuberculosis (A) in the left subclavicular region.

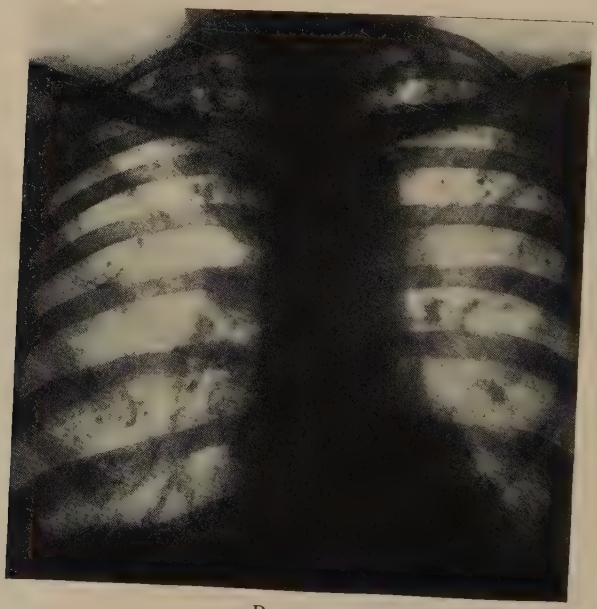

PLATE 6

Healed and calcified hæmatogenous secondary lesions (Simon's foci). In this case they are unusually numerous but show predominant apical localisation.

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is available, there is much to recommend treatment in the home. Close observation is particularly important during the first twelve months after primary infection, since during this period the majority of disseminated tuberculous lesions, including bone and joint tuberculosis and also pleurisy with effusion, occur. At present, apart from observation, the most valuable measures would seem to be regulated periods of rest, fresh air, protection from added infection, and an abundant mixed diet of high vitamin content. Cases of massive primary infection, epituberculosis, cases with constitutional symptoms, and the rare instances of multiple primary lesions are perhaps best treated in institutions, and children's sanatoria are highly suitable. In those cases of epituberculosis in which the intrapleural pressure is shown to be unduly negative, it may be desirable to institute and maintain a temporary artificial pneumothorax in an attempt to prevent the development of bronchiectasis.

Disseminated Tuberculosis.—Two important processes of widespread dissemination of tuberculosis throughout the body exist : for the bacilli may be carried in the blood-stream, or via lymphatics. Both methods may, of course, be combined. Thus, not only may lymphatic glands be infected from their own blood supply, but in the lymph the organisms may pass along the thoracic duct, and so into the subclavian vein.

Wilson estimated that tubercle bacilli could be cultivated from the blood in 5 per cent. of cases of advanced pulmonary tuberculosis, in about 2 per cent. of cases of non-pulmonary tuberculosis, and in about 36 per cent. of cases of miliary tuberculosis. Histological evidence suggests that the source of the bacillæmia is usually an incompletely healed or reactivated component of the primary complex—most commonly a caseous or liquefied mediastinal lymph gland—within or adjacent to which an intimal tubercle on a vein breaks down. Direct arterial invasion is rare. As a consequence liberated bacilli as a rule are carried back to the lungs and there may be destroyed or give rise to secondary foci. An apparently quiescent primary complex may be reactivated and give rise to disseminated lesions after many years ; occasionally, too, intermittent hæmatogenous dissemination takes place. Multiple hæmatogenous lesions from this cause more frequently occur in the first few months after primary infection. Individually somewhat rounded and small, they tend to be scattered symmetrically ; they usually heal leaving a few fibroid or calcified scars (Simon's foci) ; and they are most often found towards the apices of both lungs. Isolated large hæmatogenous foci (Assmann's foci) (Plates 5 and 6) are less common, are often situated in the subclavicular regions of the upper lobes, and are less benign, since they usually caseate and not infrequently liquefy and cavitate. Though both these types of hæmatogenous pulmonary secondary lesions may give rise to progressive phthisis, they do not themselves as a rule produce symptoms or signs. Occasionally, however, cough productive of sputum which may contain tubercle bacilli, sometimes hæmoptysis, and pyrexia with other symptoms of constitutional disturbance may occur. On the rare occasions when signs are detectable, they are limited to localised adventitious sounds. Further evidence of activity in the lesions may be obtained from observation of the sedimentation rate, or the Arneth count. Cases such as these in which evidence of activity is found need therapy based upon those principles which govern the management of phthisis (*vide* p. 95).

If tubercle bacilli are liberated into a pulmonary vein, or if, following

systemic venous dissemination, organisms pass through the capillary circulation of the lung, they will be scattered, depending on their number, more or less widespread throughout the body. Isolated or multiple foci may therefore develop if the local and general immunity is insufficient to overcome the infection. Certain sites seem more favourable for the development of progressive systemic tuberculosis than others. Thus, for example, the meninges and the central nervous system, the eye, bones, joints, the suprarenal and kidney, the epididymis and Fallopian tube, and the intestines, fairly frequently become diseased; while muscles, fascia, and tendons are rarely if ever involved. Within the organs concerned the same series of tissue reactions which has been described takes place, and their ultimate fate is bound up with the existing and resulting allergic and immunological responses of the individual. Every gradation from the most acute to the relatively chronic and ultimately healed lesion is seen. Reference should be made to the appropriate sections for further consideration of the various disorders which may result.

MILIARY TUBERCULOSIS

The hæmatogenous dissemination of a single fine suspension of tubercle bacilli may give rise to acute generalised miliary tuberculosis. Quite frequently, and when the focus of dissemination is situated in a systemic vein, the majority if not all of the lesions are situated within the lung; often the lungs and other organs share the infection; and rarely, and presumably when a pulmonary vein is originally the site whence the organisms are set free, the lungs may be spared though other organs are heavily involved.

The disorder occurs most frequently in children under ten, and it is uncommon above the age of thirty. Quite often a history of close contact with an open case of phthisis can be obtained. When miliary tuberculosis occurs in adults it is not infrequently associated with pre-existing tuberculosis of other organs, and only occasionally with chronic pulmonary tuberculosis. As a rule, however, the dissemination occurs during the first six months after primary infection. In acute cases the individual lesions—macroscopic tubercles—are predominantly exudative in type, and since the consequences of meningeal involvement are disastrous, meningitic symptoms often tend to overshadow those due to miliary tuberculosis elsewhere. It is worthy of note that, in regard to tuberculous meningitis, a curious localisation of the lesion tends to be present at the base of the brain, particularly in the neighbourhood of the interpeduncular space and about the optic chiasma. Here, beneath the thickened pia-arachnoid, a small amount of turbid exudate, which often contains tubercle bacilli, is to be found. On the membranes and along the arteries on the surface of the brain and within its folds it is often possible to demonstrate minute grey tubercles. Some degree of hydrocephalus, with flattening of the convolutions from pressure, is usually demonstrable. The cerebrospinal fluid, which on lumbar puncture is comparatively clear as a rule, but under an increased pressure, if allowed to stand, will produce a coagulum in which tubercle bacilli may be demonstrated. Before coagulation an increase of cells up to several hundred per cubic millimetre can be shown. Of these, as a rule, 70 to 80 per cent. are lymphocytes, though in the early stages higher proportions of polymorphs may be found. The protein content is increased from the normal of 30 mg. per 100 c.c. upwards to 300 mg. per

100 c.c. Glucose is diminished or absent, and chlorides will be found to be below the normal minimum level of 700 mg. per 100 c.c.

Symptoms and Signs.—Three classical types of miliary tuberculosis are described: the typhoid, the pulmonary, and the meningeal. As a rule, however, individual cases rarely conform strictly to any one type but present features of all three, with one dominant pattern. The onset is somewhat insidious, and a vague history of general impairment of health and appetite of some weeks or even months duration may be obtainable. The early symptoms are most commonly headache, vomiting, constipation, and a variable degree of pyrexia. Thus in children a gastro-intestinal upset is usually suspected, while in adults influenza is commonly diagnosed. The persistence of the symptoms, however, and the continuation of the fever, rapid deterioration in the patient's condition, with loss of weight, and then the onset of undoubted meningitis, as a rule serve to show the grave reality. As there is great variability in the clinical picture, outstanding symptoms and signs are perhaps best dealt with individually :—

1. *Pyrexia.*—Pyrexia is typically irregular, both in degree and duration. Usually wide variation between morning and evening temperature is shown, and not infrequently "typus inversus" is seen—that is to say, a pyrexia in which the morning temperature on some days is higher than that of the evening. Hyperpyrexia occurs most commonly shortly before death. Occasionally from the onset the temperature rises slowly in a "step-ladder" manner as in typhoid fever.

2. *Gastro-intestinal Features.*—Constipation and vomiting are common. The latter often occurs immediately after any food and is extremely intractable. Acetone can therefore frequently be smelt in the breath of these patients. Distension of the abdomen, in spite of constipation, does not occur; indeed, as the disease advances, its surface usually becomes scaphoid. The tongue and mouth become dry, and sordes appear around the teeth and on the lips. Diarrhœa is rarely a feature. The spleen is usually enlarged, but only occasionally to an appreciable degree in acute forms of miliary tuberculosis.

3. *Respiratory Features.*—Dyspnœa and cyanosis, disproportionately severe as compared with physical signs in the chest, are often found. The patient frequently has a cough which may be productive of small amounts of sputum, which, unless phthisis is present, only rarely contains tubercle bacilli. Scattered rhonchi and fine râles may be heard over the lungs. In addition, there may be evidence of chronic pulmonary tuberculosis.

4. *C.N.S. Features.*—Headache occurs early and is a dominant symptom, even before any other evidence of meningeal involvement is found. It is aggravated by movement, and appears to be of great intensity. The patient may cry out at intervals, even when semi-comatose. Another distressing feature of the disease is the grinding of the teeth. During the early stages irritative meningeal symptoms and signs are usually present. Thus the patient is restless, complains of photophobia, and if left alone tends to lie curled up on his side. The degree of neck retraction is usually less in tuberculous meningitis than in that due to other organisms. Neck rigidity, however, is commonly quite definite, and Kernig's sign is present. Hypertonus in the limbs, with increased knee and ankle jerks and extensor plantar responses, may be obtained. Later in the disease tendon reflexes are commonly diminished or lost, or may be absent from an early stage. Rarely,

examination of the fundi may reveal choroidal tubercles, while late in the disease papilloedema is frequently found. Cranial nerve paralyses are common, and the third nerve (squint, ptosis, and dilatation of the pupil) is often involved. In children generalised convulsions occur, and in older patients tremor and muscle spasm take place. Terminally flaccid paralysis and coma supervene.

5. *Cardio-vascular Features.*—Tachycardia from an early stage is typical, while vasomotor instability is shown by the fact that a light scratch upon the skin produces marked local erythema and a wheal (*tâche cérèbrale*).

Differential Diagnosis.—In the forms of miliary tuberculosis with prolonged pyrexia and no definite evidence of meningitis, the enteric group of fevers may be suspected. Apart from bacteriological and serological tests, however, typhoid fever commonly is accompanied by a relatively slow pulse, a fairly characteristic rash, an absence of vomiting, and a tendency of the headache to disappear after the first week. Moreover, in typhoid there is a definite leucopenia, while in miliary tuberculosis a slight leucocytosis is common. The onset of meningeal symptoms is suggestive, and the identification of choroidal tubercles conclusive proof of miliary tuberculosis. Radiological examination of the chest in an established case, furthermore, may reveal miliary foci in the lungs. In the meningeal forms there may be difficulty in the diagnosis from other forms of meningitis, or from a cerebral abscess or tumour. The posterior basic meningitis of infants is most common before the age of one, and during this period of life miliary tuberculosis is uncommon. Careful examination of the cerebrospinal fluid is diagnostic, in that the organism concerned can usually be identified with certainty. Moreover, in tuberculous meningitis the increase in cells is commonly mainly lymphocytic, while a marked fall in the chloride content is very characteristic. Sometimes encephalitis lethargica or anterior poliomyelitis may be suspected, but in both these conditions the increase in cells in the cerebrospinal fluid is commonly less marked than in tuberculous meningitis, and the subsequent course entirely different. Careful examination of the tympanic membranes is essential, since the early stages of sinus thrombosis or meningitis arising from middle-ear disease may give symptoms somewhat similar to miliary tuberculosis. It is worthy of note that the tuberculin skin reactions are of little or no help in diagnosis, since they are commonly negative in miliary tuberculosis.

Prognosis.—In almost every case the disease is fatal, and the duration of life from the onset of the symptoms varies from a few days to a few months. Cases which run a subacute or chronic course are encountered, and isolated instances of recovery from miliary tuberculosis are on record.

Treatment.—Palliative therapy consists in the relief of headache by frequent lumbar punctures ; the exhibition of sedatives, including morphia ; and the employment of such comforts as a darkened room, an absence of noise and of disturbance of the patient, are all important. Persistent vomiting may make nasal feeding necessary. No measure is yet known to make any major difference to the progress of the disease, though early reports of the use of streptomycin are most encouraging.

Chronic Miliary Tuberculosis.—Hoyle and Vaisey have described a group of cases in which evidence of miliary tuberculosis was obtained and in which the patients lived for more than six months. Occasional cases apparently healed their lesions and recovered. The outstanding features of the disease

were the following : prolonged irregular toxæmia with recurrent phases of pyrexia associated with sweating, anorexia, loss of weight, amenorrhœa, cough, and sometimes pleuritic pain. Splenomegaly, generalised enlargement of lymph glands, tuberculides of the skin, iridocyclitis, cystic changes in the small bones of the hands and toes, and occasionally uveoparotitis, are all variously found. The radiological appearances within the chest may show a distribution of foci similar to that in the common acute form of the disease. Not infrequently, however, the appearances suggest gross mediastinal lymphadenitis, together with a reticular shadowing spreading out throughout both lungs. When death occurred in these cases, it commonly did so after many months of toxæmia, and post-mortem findings were those of generalised disseminated tuberculosis. It is very often extremely difficult to demonstrate tubercle bacilli in these cases, and so in life the diagnosis often remains a matter of some doubt. Moreover, conditions such as sarcoidosis, tuberculous broncho-pneumonia, and silicosis may on occasion give somewhat similar clinical or radiological features.

Therapy is palliative and symptomatic, but should be associated in every case with prolonged rest, abundant good food, and, if recovery seems possible, a sanatorium regime at a later stage.

Lymphogenous Disseminated Tuberculosis

(*Glandular Tuberculosis*)

The structure of the lymphatic system with its intercalated lymph glands and numerous interglandular lymph vessels, the low pressure obtaining within these vessels, and the temporary fluctuations in the direction of flow of lymph make possible a relatively slow dissemination of tuberculosis widely throughout the body.

Primary tuberculous infection with consecutive involvement of the regional lymph gland commonly in turn leads to more or less extensive infection of neighbouring lymphatics and the glands into which they drain. Temporary or permanent arrest of the process may take place at this point, and the tissue reactions associated with healing occur. Sometimes, however, dissemination continues until virtually generalised lymphatic glandular tuberculosis results. Not infrequently reactivation of glandular disease after a variable period of arrest is followed by further extension. Since the general direction of lymph flow is centripetally towards the thorax, the spread of the disease from peripheral primary foci in, for example, the intestines or tonsil tends to be in that direction. Secondary hæmatogenous lesions in viscera and the adult type of pulmonary tuberculosis seem rarely if ever of themselves to give rise to lymphatic glandular tuberculosis, though direct hæmatogenous spread to lymph glands undoubtedly occurs. On the other hand, hæmatogenous spread from an infected gland is a persistent possibility. Apart from this risk, the disease is relatively benign, and it is possible that considerable immunity to tuberculosis later in life may thereby be developed. In England, children between the ages of four and twelve are predominantly affected, though the disease is by no means rare in adolescence and young adult life. A high proportion of cases, when mesenteric or cervical glands are outstandingly involved, are due to bovine tubercle bacilli. The relative preponderance of cases in which cervical glands seem exclusively concerned

is more apparent than real, and is due to their superficial situation, for in fact the mediastinal glands are by far the most commonly infected group.

The appearance of the child with active glandular tuberculosis often suggests the "tuberculous diathesis," with its clear beautiful complexion, marked hirsuties, and long eyelashes. Sometimes in children, and commonly in young adults, extensive glandular post-primary tuberculosis is associated with cutaneous striæ and occasionally petechiæ.

Recurrent pyrexia, sweating, loss of weight or failure to gain weight, malaise, and lassitude may occur independently of the site of the glands involved. The clinical features otherwise depend on the localisation of the adenitis. Thus, in the neck, superficial enlargement may be visible and palpable. Such glands are commonly matted together and to surrounding structures, including the skin. The latter may be eroded and a discharging sinus form, which takes a long time to heal and may cause extensive scarring. Pain and tenderness are usually inconspicuous, until secondary infection takes place. When caseous, the glands are hard to palpation; with liquefaction which may itself be associated with secondary infection from tonsils or teeth, the mass may feel cystic. Calcified glands feel like small flints.

Mesenteric tuberculous adenitis is commonly symptomless, but if extensive may give rise to progressive debility, asthenia, stunting of growth, pain, anæmia, and persistent diarrhœa with fatty or watery stools. The abdomen may be distended, and associated tuberculous peritonitis is not uncommon. The mass of glands may be palpable, while, with healing, intestinal obstruction may occur.

Local symptoms associated with mediastinal lymphadenitis are cough, and occasionally pressure symptoms on mediastinal structures such as veins or bronchi. Bronchial obstruction from this source causes pulmonary atelectasis and leads ultimately to bronchiectasis in a considerable number of cases. Liquefaction within these glands leads to the formation of a mediastinal abscess in rare instances.

The physical signs of enlarged mediastinal glands described by d'Espine and Eustace Smith are inconstant, and diagnosis is largely dependent upon symptomatology and X-ray examination. Calcification is very characteristic.

Tuberculous lymphadenitis must be distinguished from Hodgkin's disease, the leukæmias, lymphosarcoma, neoplastic disease, sarcoidosis, and syphilis. Less commonly, chronic pyogenic adenitis, glandular fever, cœliac disease, and sprue may resemble the condition. The age, history, and appearance of the patient; the local characteristics of the glands, if these are accessible, or their radiological appearances if within the thorax; the state of the blood and spleen; the presence of foci of infection; a positive Mantoux reaction; and, if possible, histological examination of an excised gland, will usually permit diagnosis.

Treatment for the most part consists of rest, good surroundings with fresh air, and good food. Graduated exposure to sunlight or ultra-violet light, cod or halibut liver oil, and, if necessary, extra vitamins B and C, and iron or liver extract depending on the type of anæmia present, are often of value. Cervical glands are sometimes best treated by X-ray therapy, especially at an early stage, while their surgical removal is also often successful and may prevent the formation of an unsightly sinus.

PULMONARY TUBERCULOSIS

(*Adult Type*)

Pathogenesis.—Ranke's theory of the three immunological stages of tuberculosis, and the work of Redeker in the Ruhr in 1921-28, led in Germany to the elaboration of a complex hypothesis as to the development of phthisis which has gained acceptance in most European countries and in the U.S.A. In broad outline, on this view phthisis rarely if ever develops directly from primary infection, but begins characteristically with a new infiltration in a previously infected and usually adult individual, probably often by hæmatogenous spread from a mediastinal gland, though also possibly by exogenous reinfection. This new lesion, it is thought, only progresses if a state of hypersensitiveness to tuberculin overshadows the immunity of the individual. Alternation in the dominance of allergy and immunity thereafter determine the fate of the lesion.

It is generally agreed that the common earliest recognisable pulmonary lesion from which phthisis develops is an isolated focus which appears abruptly, often in the upper and posterior part of the lung. The lesion may progress rapidly in size, and similarly may cavitate at an early stage and thus give rise to further lesions by bronchogenous extension of the infection. Less frequently, however, phthisis has been shown to develop from reactivated primary or secondary lesions ; while occasionally subacute or chronic miliary lesions may become confluent and cavitate, and so give rise to the disorder. In Scandinavia it is held that progressive pulmonary tuberculosis not infrequently develops directly from the acute primary pulmonary lesion. In the author's opinion this method of development of phthisis is common in this country, particularly when primary infection occurs in adolescence or adult life.

Symptomatic pulmonary tuberculosis of the adult type is only rarely seen in children. Above the age of fourteen, however, it becomes increasingly common, the highest case-incidence occurring between nineteen and twenty-five. The morbidity rate falls again in succeeding years, but even those of advanced age are not infrequently subject to the disease. Radiological and fluorographic surveys of large populations have shown that the prevalence of this disease in the apparently healthy increases with age up to a maximum at forty-five years, and that thereafter a constant level is maintained.

Pathology.—The tissue reactions occurring within the lung in chronic pulmonary tuberculosis have been described. Certain pathological features, however, need emphasis. Extension of the lesions within the lung may occur by recurrent hæmatogenous spread, or more commonly by bronchogenous dissemination of the infection from excavated pre-existing foci. The size of the cavity, once a bronchus has been eroded, is largely determined by the mechanics of the air entry into it. A pull is exerted peripherally upon its walls by the elastic retraction of the surrounding lung tissue. If the bronchial opening becomes partly occluded by debris or by kinking, and so permits air to enter the cavity on inspiration more easily than it allows egress on expiration, rapid increase in size of the cavity will take place until the partial obstruction is overcome or becomes complete. In the latter case air is slowly absorbed into the blood stream and the cavity tends to close. Fluctuations in size not uncommonly take place fairly quickly. Permanent closure of the cavity may

follow in this way, or sometimes may take place if it becomes entirely choked by caseous debris ; while uncommonly epithelialisation of its walls takes place with healing of the tuberculous process, and a functional bronchiectatic excavation remains. Usually, however, in an untreated case, the cavity persists; bacilli are aspirated into adjacent areas of the lung and the disease slowly extends. Healing reactions may take place, or may be interrupted by fresh bronchogenous or hæmatogenous spread. Commonly a slow, irregularly progressive extension of the disease throughout both lungs is seen. In such cases associated tuberculous lesions of the larynx and of the intestines may develop. Not infrequently, also, and especially in advanced cases, amyloid disease develops, involving as a rule the spleen, liver, kidneys, or intestines.

At autopsy in a typical advanced case the body is emaciated. On opening the thorax, the visceral and parietal pleuræ are found to be more or less adherent. Adhesions between the lobes are always found, and the pleura at the apices is usually thickened. The affected areas of lung are diminished in size and the remainder is enlarged by compensatory emphysema. The heart and trachea are displaced towards the more shrunken lung. The lungs themselves, often greatly disorganised, may contain little tissue capable of physiological function. They show in different parts various associated changes, *i.e.*, atelectasis, bronchiectasis, tuberculous tracheo-bronchitis, fibrosis, caseation, cavitation, healed calcified foci, and areas of productive tuberculous inflammation.

Classification.—In the British Isles the classification in use is that suggested by the Ministry of Health in 1930. Four groups are separated as follows :—

Grade A : Cases in which tubercle bacilli have never been demonstrated in the sputum, pleural fluid, fæces, etc. Grade B : Cases in which tubercle bacilli have at any time been found. This Grade is subdivided into three sub-groups. Grade B1 : Cases with little if any constitutional disturbance, exhibiting limited physical signs, and having no complications (tuberculous or other). Grade B3 : Cases with marked constitutional disturbance, severe impairment of function, either local or general, and with little or no prospect of recovery. This grade includes all cases having grave complications, such as diabetes mellitus, tuberculous enteritis, etc. Grade B2 : All cases which cannot be placed in Grades B1 or B3.

Tuberculosis Surveys.—The investigation of the apparently healthy has shown that in this way only may we hope to diagnose pulmonary tuberculosis in its earliest stages (when therapy is most effective) in a high proportion of cases ; for the disease at its onset and for long thereafter may cause no noteworthy symptoms. The available methods in use include tuberculin reactions, the significance of which has been discussed, fluorography, and radiography. Fluorography is economical and time-saving and will probably be used increasingly for large sections of the population. Yearly re-examination of the normals is desirable, and when any significant abnormality is disclosed full investigation is essential.

Early Symptoms.—The onset of pulmonary tuberculosis may be insidious, or it may be characterised by striking symptoms which the most unobservant patient cannot overlook. It is commonly stated that the cases presenting a sudden onset are those with the best chance of recovery ; such patients often submit themselves for treatment at an early stage of the disease. It is there-

fore most important that these early symptoms should be recognised in their true significance by all. A common mode of onset is an acute transient febrile illness accompanied by respiratory catarrh and malaise, the illness resembling influenza. The most outstanding of these early manifestations of the disease are hæmoptysis and pleurisy. These are also common in the later stages of the disease, but their value in diagnosis arises from the fact that they sometimes occur months before any other definite symptom of pulmonary disease, and long before the lesion in the lung is sufficiently extensive to present physical signs or even to be discoverable by X-ray examination.

Hæmoptysis.—This is the first symptom in about 10 per cent. of cases of phthisis. In its most characteristic form it occurs as a sudden free hæmorrhage "out of a blue sky." The patient, while apparently in perfect health, may one day feel warm fluid in his mouth and expectorate perhaps as much as half a pint of bright red blood. During the succeeding twenty-four hours he coughs up clots of darker blood mixed with mucus, thus demonstrating that the site of the bleeding is in the lungs. Such an event demands the fullest investigation and close observation. Hæmoptysis occurs in a variety of other conditions, but only in early phthisis do we get sudden copious bleeding in a patient who is apparently well and who is not the subject of cough, expectoration, or dyspnœa.

Pleurisy.—Pleural effusion in an adult should be regarded as a tuberculous disorder in the absence of some other demonstrable cause, such as pneumonia or cardiac disease. The fluid in tuberculous pleurisy is clear, sterile, and contains lymphocytes.

Dry pleurisy is of less significance, and is often non-tuberculous. It is, however, a frequent forerunner of phthisis; in tuberculous cases it is usually recurrent and accompanied by pyrexia, which subsides when the patient is confined to bed but recurs when he is allowed up.

Even in the absence of dramatic symptoms a careful analysis of the complaints of the patient will sometimes enable us to diagnose the disease before it is advanced. The characteristic symptoms are: (i) excessive fatigue—the patient is exhausted by an ordinary day's routine which he could formerly accomplish without discomfort; (ii) loss of weight—this may not be rapid but it is continued, and after a few months will be noticed by his friends; (iii) failure of appetite—in many cases the patient will state that his appetite is good, but when asked what he eats for breakfast he will almost invariably admit that he has no desire for food in the mornings; (iv) amenorrhœa—in young women irregularity or cessation of menstruation is a very common symptom of early phthisis; (v) excessive sweating; the most characteristic example is the night-sweat which occurs during deep sleep in the early hours of the morning and involves the whole of the skin area; equally common in early phthisis is axillary hyperhidrosis, which occurs during the day and soaks through the clothes in the arm-pit, even during the coldest weather. Axillary sweating is, however, not infrequent in nervous subjects under the influence of emotion.

The above symptoms are of toxæmic origin. Cough and expectoration are pulmonary symptoms often accompanying the onset of phthisis. The more important symptom is expectoration; if this persists for a number of weeks in an adolescent it should arouse suspicion of tuberculous disease. *Repeated* microscopic examinations of the sputum are essential and should if necessary be supplemented by culture or guinea-pig inoculation.

Physical Signs of Early Phthisis.—*Fever.*—Observation of the temperature range while the patient is up and about will show an abnormal diurnal variation in many early cases. The temperature may be recorded in the mouth or the rectum. Mouth readings are reliable if taken with care in patients who are not dyspnœic and who are not mouth breathers. In phthisical patients it will often be found that the morning temperature is unnaturally low, and that during the afternoon or evening it rises above normal to the extent of half a degree Fahrenheit or more. In women undue attention should not be paid to records taken during the week preceding menstruation, as many healthy women show a slight rise of temperature at that time.

Tachycardia.—The pulse-rate is very often quickened in early phthisis, even when the patient is apyrexial. A pulse-rate persistently below 80 beats per minute is presumptive evidence against a diagnosis of progressive tuberculosis.

Signs in the Chest.—In its early stages pulmonary tuberculosis is not usually accompanied by abnormal physical signs in the chest, and consequently radiological and other investigations should never be withheld in cases where the symptomatology is suggestive because the lungs appear normal to routine physical examination. However, in established but not necessarily advanced disease, on *inspection* wasting of muscles over the back of a diseased apex may be found. The muscle most affected is usually the supraspinatus; indeed most of the abnormal signs will be found posteriorly. Later, in many cases, there is also falling in of the soft parts above and below the clavicle. Diminished movement of the upper chest may also be detected.

Light *percussion* may reveal impaired resonance at the apex of the lung. The note obtained over corresponding points on the two sides should be compared while the patient holds his breath with the lungs fully inflated. The most important situations for percussion in front are above the clavicles, below their outer thirds, and direct percussion on the shafts of these bones. Posteriorly the apex should be percussed over the first and second interspaces. In normal subjects it is not uncommon to find the right apex less resonant than the left in front, but any such difference over the posterior aspect of the upper chest is of pathological significance. Impairment of resonance is sometimes met with at an early stage of the disease at the top of the axilla, or in the region between the vertebral column and the inner border of the scapula.

Auscultation.—In early phthisis the breath-sounds in the neighbourhood of the lesion are sometimes feeble. During ordinary breathing no added sounds may be audible, but accompanying or immediately after a cough crepitations or fine râles are often to be detected. Bronchial or tubular breathing is not heard over small areas of infiltration.

The spoken voice will be conducted normally; pectoriloquy will only be obtained with a considerable area of consolidation or a cavity and is not, therefore, an early sign.

Symptoms and Signs in Later Stages.—In the later stages the toxæmia is shown by a hectic swinging temperature which may range from 97° F. in the morning to 102° F. at night. Moreover, the pyrexia which at first was only present when the patient was up can no longer be subdued even by prolonged rest in bed. The body is wasted, the cheeks flushed, the eyes bright and sunken, the lips dry. The fingers may be clubbed, the nails being thin and dull, in these respects differing from the very thick polished nails seen on the

clubbed fingers of the bronchiectatic. The breath has a peculiar stale sweetish odour, not grossly offensive as in lung abscess; the sputum is copious, purulent, and nummular, *i.e.*, it floats in separate rounded lumps in the sputum-cup. Dyspnœa and cyanosis may be well marked.

The voice may be husky if laryngitis has developed, while dyspepsia, constipation, or diarrhœa may arise either reflexly or as a result of tuberculous enteritis.

As the disease advances, weakness and languor increase, the appetite does not fail completely, but it becomes capricious and the patient feels a craving for unusual and highly seasoned dishes. Sleep is disturbed by the frequent cough and copious expectorations, also by profuse night-sweats. The mentality remains clear to the end, and the patient complains little unless he be tortured by the pain of severe laryngeal ulceration. There is often an unnatural sense of well-being and hopefulness of recovery, the *spes phthisica* of the older writers.

Besides the retraction of the upper parts of the thoracic wall and displacement of the mediastinum, immobility over the diseased areas of lung will be noted. Over-extensive infiltration movement and air entry are often restricted, expiration prolonged, and râles and rhonchi may be audible, especially after coughing. Consolidation is characterised by impaired resonance, bronchial breathing, pectoriloquy, and crackling râles; fibrosis and atelectasis by poor movement and air entry, a prominent sternomastoid muscle, impaired percussion note, and mediastinal displacement towards the affected side. Over a cavity characteristic signs may be obtained if it is both large and superficial. In these circumstances tympanitic resonance may be obtained in the centre of an area of dullness, with amphoric breath sounds and crackling râles. Whispering pectoriloquy is strikingly obvious, and not infrequently it sounds as though two persons were whispering in unison, a sign known as "echoing pectoriloquy." With small cavities or even large ones that are not superficial, these characteristic signs are absent, and either no abnormal signs, or only those of surrounding infiltration or fibrosis, may be obtained.

Course.—The progress of a case of chronic ulcerative tuberculosis is usually one of alternate remissions and exacerbations. Adequate treatment in the early stages may bring about quiescence and arrest of the disease, but even while under treatment serious relapses occur, sometimes apparently dependent on undue exposure to the sun's rays, sometimes associated with an indiscreet resumption of increased exertion, or following hæmoptysis. Most frequently, however, no cause can be found to explain the relapse. After the disease has been arrested it may again become active as a result of other diseases, of an unhygienic mode of life, or of any factor which lowers resistance, and in women one of the common causes of reactivation is pregnancy. On the other hand, there are many cases in which the disease, though never arrested, dies down to a low grade of smouldering activity for months or years at a time. During these periods of remission there may be no pyrexia and little toxæmia, although the sputum may teem with tubercle bacilli.

Modes of Death.—A fatal termination is most commonly brought about by a gradual failure of strength, the result of poisoning by the toxins of the tubercle bacilli and of increasingly impaired respiration. Hæmorrhage is not often the immediate cause of death, but rupture of an aneurysm in a tuberculous cavity brings some cases to an abrupt end, the patient drowning in his own blood.

Not infrequently death is due to extension of the disease to other organs ; ulceration of the larynx with severe dysphagia may prevent the swallowing of food, ulceration of the intestines may cause exhausting diarrhœa, or the entry of bacilli into the blood stream may lead to miliary tuberculosis.

Other Varieties of Pulmonary Tuberculosis

Fibroid Phthisis.—This variety of the disease is characterised by the formation of much fibrous tissue in the affected areas of the lungs, accompanied by atelectasis. The diseased areas are shrunken, the pleura is thick and adherent, and elsewhere the lungs are enlarged by compensatory emphysema. Physical examination reveals clubbing of the fingers, retraction of the chest wall, and displacement of the heart and trachea towards the more affected lung, and often a striking variety of signs dependent upon excavation, atelectasis, fibrosis, and bronchiectasis. The disease runs a very chronic course with little pyrexia or constitutional disturbance. The patient may be dyspnœic and cyanosed. Tuberculous tracheo-bronchitis, and enteritis often develop. Repeated hæmoptyses are common. After many years of slight ill-health the end may come fairly quickly as a result of heart failure, amyloid disease, or hæmoptysis.

Tuberculous Pneumonia.—Tuberculous pneumonia is uncommon save in young subjects. The disease often proceeds to a fatal termination in a few weeks or months, without any remission. In the lungs the changes may take the form of a caseating lobar pneumonia, with which there is little protective formation of fibrous tissue (*vide* Plate 8). In other cases the pathological changes are those of broncho-pneumonia, with patches of consolidation scattered over both lungs. In the latter type the physical signs are at first those of a diffuse bronchitis ; tubular breathing and crackling râles give evidence of areas of consolidation after a week or two. Liquefaction with excavation is common in each form, as is atelectasis in the less acute cases. Broncho-pneumonic phthisis not infrequently follows a brisk hæmoptysis.

Symptoms.—There may occur a prodromal stage of vague ill-health lasting several weeks, then a sudden exacerbation with chill, fever, pleuritic pain, and cough. The patient is forced to remain in bed by weakness and dyspnœa. Sustained or remittent high pyrexia occurs together with rapid emaciation. The sputum may at first be frothy and blood-stained, but it soon becomes green and nummular and swarms with bacilli. In the great majority of cases death results from toxæmia within a few months, and the disease is not usually improved by collapse therapy.

Senile Phthisis.—Pulmonary tuberculosis is quite common in elderly subjects, and is a frequent cause of death in inmates of almshouses and other institutions for the aged. The course is variable, but no treatment is effective in arresting its progress. Both the symptoms and the physical signs are often masked by accompanying bronchitis and emphysema. Fairly typical X-ray appearances are shown on Plate 9.

Complications of Pulmonary Tuberculosis. — *Secondary Infections.* — Bronchi in diseased areas in the lungs are often secondarily infected, and if cavities are present the toxæmia from these secondary infections may overshadow the symptoms due to the original tuberculous disease. The organisms commonly found are the *Staphylococcus aureus*, pneumococcus, and streptococcus.

PLATE 7

Chronic pulmonary tuberculosis. Extensive fibrosis and excavation of the right upper lobe has occurred and there has followed a secondary spread into the middle zone of the left lung.

[*To face page* 92.

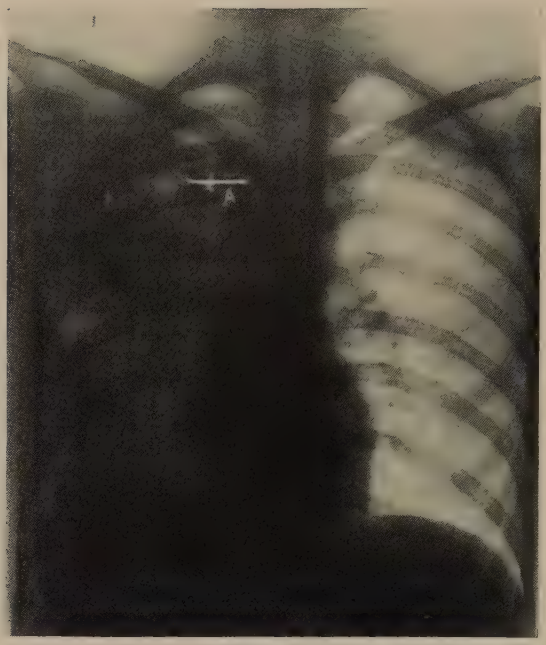


PLATE 8

Tuberculous pneumonia involving nearly the entire right lung. Excavation is just beginning at A.

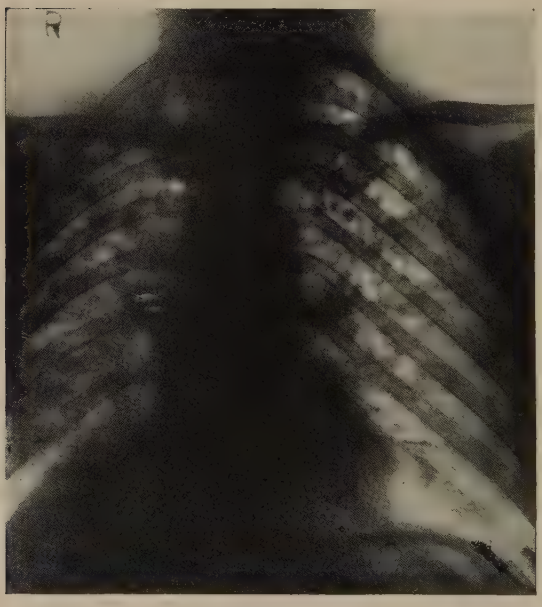


PLATE 9

Senile phthisis, showing extensive bilateral infiltration and fibrosis with little or no excavation.

[*To face page* 93.

Lungs.—Pulmonary atelectasis widely varying in degree commonly complicates pulmonary tuberculosis. In well-marked cases the paucity of the symptoms, and the relatively chronic course of the disease, contrasts strongly with the apparently gross physical signs and striking radiological appearances. The sputum in such cases as a rule persistently contains tubercle bacilli. Bronchiectasis far more frequently complicates phthisis than is usually suspected, as also does tuberculous tracheobronchitis.

Pleura.—The pleura never escapes inflammatory change, and in the majority of cases there are found thickening at the apex and adhesions uniting the lobes of the lung to one another, and attaching them to the chest wall. Rupture of an adhesion may cause spontaneous pneumothorax, hydro-pneumothorax, or tuberculous empyema.

Infection of Tissues by Sputum.—The passage of infected sputum may lead to tuberculous ulceration of the larynx or of the tip of the tongue. If the sputum is swallowed the infection will be carried down the alimentary tract, and may cause intestinal tuberculosis. The Peyer's patches of the ileum will be chiefly affected.

Fistula in ano is very often secondary to pulmonary tuberculosis, and is of special interest, as it is a complication which may occur early in the disease, sometimes long before the patient is aware that he has a lesion in the lung.

Metastatic Complications.—Hæmatogenous dissemination, though much commoner after primary infection, may occur and may give rise to miliary tuberculosis, or may lead to the development of tuberculosis in, for example, the central nervous system, heart, kidney, epididymis, suprarenal, or one of the larger joints.

Amyloid Disease.—The prolonged toxæmia may cause amyloid degeneration of the solid viscera or bowel. Clinical evidence of this complication appears as œdema, diarrhœa, profuse albuminuria, and enlargement of the liver and spleen.

Prognosis.—There is no disease in which prognosis is more difficult, and there is an old saying that " he who attempts to forecast the outlook may be sure of one thing only, that he will be mistaken." Autopsy experience shows that the disease may heal at almost any stage. There are, however, certain factors which help us to form an estimate as to the chances of recovery, or, failing this, of the probable duration of life.

Type of Disease.—Cases of acute miliary tuberculosis are as a rule fatal, and tuberculous pneumonia almost equally hopeless. In the other types, those cases in which there is a predominance of fibrotic change or atelectasis are more hopeful than those in which the disease is mainly exudative. Eighty per cent. of those with unclosed cavities die within five years. The disease may become arrested, and apparent health may occasionally be maintained for years in spite of cavitation.

Extent of Damage in the lungs is not a reliable guide to prognosis; the rate at which the destructive process advances is of much greater significance and is shown by radiological examination.

Toxæmia.—Pyrexia not quickly subdued by rest in bed is of grave import, as is tachycardia, even without pyrexia.

Age, Habits, and Constitution.—An unfavourable course must be expected if symptoms occur below the age of eighteen or above that of fifty years. Effective treatment and after-care may be impossible if the patient is of an impatient temperament or low intelligence, or if his financial resources

are insufficient to provide adequate rest and nourishment. Alcoholism is always a most unfavourable feature. The prognosis is more grave in those of Irish or Scots descent than in Jewish or English patients. A family history of the disease is similarly an adverse factor.

Presence of Complications.—Ulceration of the larynx or of the bowel add very greatly to the gravity of the outlook in any stage of the disease, but do not necessarily make it hopeless. Diabetes mellitus, silicosis, and pregnancy may seriously aggravate the disease.

Diagnosis.—It is of the utmost importance that pulmonary tuberculosis should be recognised at an early stage. The chance of arresting the disease may be irrevocably lost if treatment is delayed for several months. Delay in diagnosis is common for two reasons; firstly, because the onset is often insidious and patients do not seek advice until the disease has become firmly established; secondly, because practitioners wait for the appearance of physical signs in the chest before committing themselves to a diagnosis. The increasing use of fluorography should diminish the consequences of the first, the second should not arise.

If the onset is heralded by dramatic symptoms such as hæmoptysis or pleurisy, the practitioner should insist upon early and adequate investigation. When the onset is insidious the diagnosis is based on a careful synthesis of the symptoms and history. Absence of a history of contact with the infection is of no significance. Confirmation is sought by observation of the daily range of temperature; afternoon pyrexia may be present only if the patient is allowed to take exercise. It is characteristic of tuberculous toxæmia that a brisk two-mile walk will raise the temperature unduly, and that it will not subside to normal within thirty minutes.

The most satisfactory proof of the diagnosis is the demonstration of tubercle bacilli in the sputum. If the first examination is negative, it should be repeated several times, and attempts should be made to culture the organism; in cases where there is no expectoration, the bacilli should be searched for in the gastric residue. Various sputum-concentration methods or the examination of a laryngeal swab may also be of assistance in finding the organism.

In every case in which pulmonary tuberculosis is suspected *efficient radiological examination of the chest is essential.* Repeated radiological examination is equally necessary as a guide to treatment once the diagnosis has been made. The earliest lesions of adult type tuberculosis are commonly situated posteriorly in the subapical areas, or in the apex of a lower lobe.

The common appearances of adult type pulmonary tuberculosis in radiographs are: (i) Infiltration, which takes the form of fluffy opacities with ill-defined margins localised or scattered over the lung fields without apparent relation to the arrangement of the vessels or bronchi; (ii) Cavitation, which is seen as a more or less dense ring-shadow, the lower part of which may show a "fluid level"; (iii) Larger confluent opacities of varying size; (iv) Fibrotic strands, or thickened pleura; (v) Lobar, or lobular atelectasis, with mediastinal displacement; and, (vi) in arrested disease, Calcification.

Tomography will show that the bulk of the lesions are situated posteriorly and may help in the localisation of cavities.

None of the physical signs elicited by examination of the chest are diagnostic of pulmonary tuberculosis. However, abnormal signs in the above-mentioned regions are suggestive and help to confirm other evidence.

Active and Inactive Pulmonary Tuberculosis.—The presence of tubercle bacilli in the sputum is certain evidence of activity. In the absence of such a finding active disease may be presumed if (i) radiological evidence of pulmonary tuberculosis exists and, in addition, any one or more of the following are present; (ii) undoubted symptoms and signs of active disease, *e.g.*, pyrexia, loss of weight, anorexia, night-sweats, etc.; (iii) otherwise unexplained persistent elevation of the sedimentation rate; (iv) altering tuberculous radiological appearances on serial examination, particularly if fresh infiltration or excavation should appear.

Differential Diagnosis.—A variety of conditions may be mistaken for pulmonary tuberculosis, both in its early and later stages.

Various forms of pneumonia may simulate pulmonary tuberculosis clinically and even radiologically, but usually the diagnosis becomes clear if the patient is kept under observation. It is seldom justifiable to diagnose pulmonary tuberculosis on a single X-ray of the chest unless other findings support the diagnosis.

Hyperthyroidism and Anxiety Neurosis may simulate early phthisis with symptoms such as tachycardia, loss of weight, and amenorrhœa, but do not cause the remittent pyrexia of phthisis.

Hæmoptysis is common in *mitral stenosis*, *bronchiectasis*, *lung abscess*, and *bronchial neoplasm*.

Clubbing of the fingers with pyrexia and tachycardia may be due to *subacute bacterial endocarditis*. Malaise, pyrexia, tachycardia, and loss of weight are associated with some generalised infections such as undulant fever, and sometimes with focal sepsis such as chronic sinusitis, and the latter may provoke recurrent or chronic bronchitis.

In most cases of chronic pulmonary tuberculosis repeated examinations of the sputum will reveal tubercle bacilli; elastic fibres may be found in the sputum in cases of pulmonary tuberculosis and pulmonary suppuration. If purulent sputum is produced, and tubercle bacilli cannot be demonstrated after repeated search, the diagnosis is unlikely to be pulmonary tuberculosis.

Treatment of Pulmonary Tuberculosis

Effective chemotherapy or immuno-therapy are not available for this disease. Treatment, therefore, is limited to measures which have as their object the diminution of toxæmia and the promotion of natural healing of the lesions. Long experience has shown that of these measures rest is fundamental, and that whole-hearted co-operation by the patient is essential for success.

As soon as the diagnosis has been made the patient should be confined to bed for a period of complete rest. This rest period may be carried out in the patient's home, in a well-ventilated room, under the supervision of a trained nurse. No restrictions are placed on diet except as regards alcohol; meals should stimulate the appetite, should be small and frequent, and should include abundance of milk, butter, and raw fruit. The calorie value of the diet will depend upon the amount of activity permitted but should in general be high. Cod-liver oil and Vitamin C may be given throughout the whole period of treatment and during the winter months for several years after. If the patient is poor, or if the home conditions are otherwise unsuitable, he must be placed in a hospital. He should not be in contact with non-tuberculous patients, especially children.

The activity of the tuberculous lesions is assessed repeatedly by the aggregate evidence which symptoms, signs, temperature, repeated X-ray and sputum examinations, and such tests as the blood sedimentation rate and a differential leucocyte count present. Every endeavour should be made to persist with complete rest until all evidence of active disease has disappeared. This principle applies whatever other treatment may be used in every case for which hope of recovery exists.

Sanatorium Treatment.—Sanatorium treatment is in general suitable for early and a high proportion of moderately advanced cases of pulmonary tuberculosis. The patient and his relatives require reassurance on two points : firstly, may not residence at a sanatorium stamp the inmate as a consumptive and render him an object of dread for the rest of his life ; secondly, when at the institution will he mix with patients in a more advanced stage of the disease from whom he may contract a more virulent infection. Neither of these suppositions is correct. Sanatoria do not broadcast the names of their inmates ; moreover, notification of all cases of active tuberculosis is the statutory duty of every practitioner whether the patient goes to a sanatorium or not. Furthermore, a patient who is suffering from the disease is believed to be relatively immune to reinfection, and training in preventing the spread of infection is part of the sanatorium regime.

Provided that careful skilled attention is available, the situation and climatic conditions are of secondary importance. Careful consideration of the financial consequences of a prolonged stay must be undertaken beforehand ; while factors such as the age, temperament, the social position of the patient, and the difficulty of the journey involved are also important in this decision. Financial support to the family of the patient when needed is increasingly becoming a State liability.

General Principles of Sanatorium Treatment.—Throughout his stay in the sanatorium the patient is encouraged and studied. When to the above criteria his lesions seem inactive, rest is modified and minor activities are gradually permitted. He is later slowly inured to an outdoor existence, and is allowed up for increasing periods. He is permitted to take more and more exercise, and finally graduates to manual labour. If pyrexia recurs at any time, the patient reverts to complete rest, and when inactivity of the disease may again be presumed he is worked up through the various grades of physical exertion once more. Occupational therapy and training for a modified life in the future are very often essential.

He is educated in a strict routine which he is to follow for the rest of his life. This includes intolerance of unventilated rooms, avoidance of heavy clothing both by day and night, regular periods for rest and meals, avoidance of hurry, fatigue, and excitement. If there is sputum he is taught to dispose of it in such a way that it may not be a danger to others, and he is trained not to swallow it lest it should infect his own alimentary tract.

After-care.—On leaving the sanatorium the patient should be kept under regular clinical and *radiological* observation for several years. If he is a wage-earner he must be advised as to possible modifications of his work in order that he may avoid long hours and periods of stress, without reducing his earning capacity to the level of privation. Some financial support from the State or other source is commonly desirable at this time. A change of employment from a sedentary occupation to laborious work out of doors is seldom advisable. Female patients must be warned to avoid the risk of pregnancy

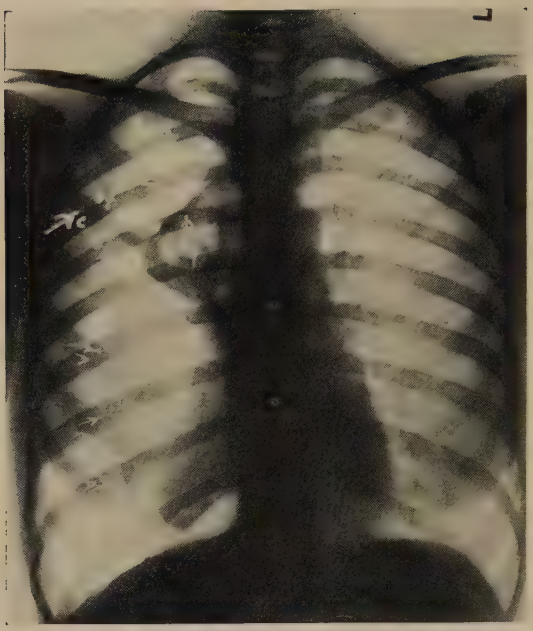


PLATE 10

Right artificial pneumothorax, showing the lung edge (A) and an uncollapsed cavity (B) in the right upper lobe held out by adhesions (C).

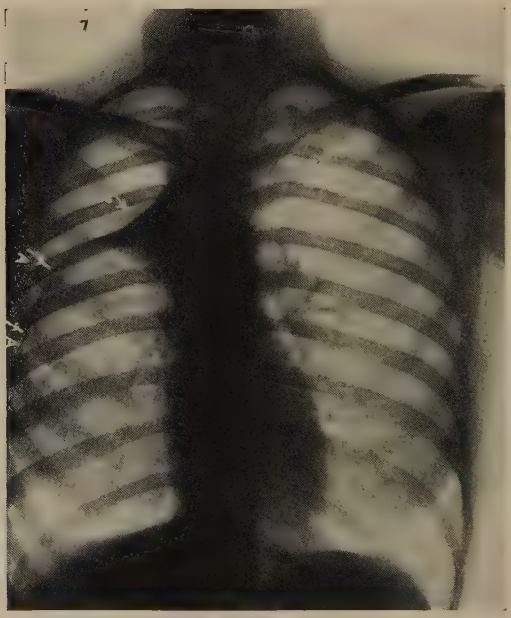


PLATE 11

The same case after the adhesions have been divided. The lung edge is visible at A. The diseased area shows complete selective collapse.

[*To face page* 97.

until to every available test the disease has been arrested for four or five years.

Accessory Methods of Treatment.—If toxæmia cannot be controlled by complete rest in bed, if the disease is advancing rapidly, or if relapse takes place during or shortly after the routine measures just described, other methods must be employed. The most effective of these are described under the term " collapse therapy."

Collapse Therapy.—The principle underlying this treatment is comparable with the usual method of dealing with tuberculous arthritis, which is to secure immobilisation of the inflamed parts. With respiration the lungs are moved and stretched continually, and the flow of blood, lymph, air, and sputum through them is modified and varied. The process may impede the healing of lesions, and disseminate toxins and organisms. It is possible, relatively or absolutely, to immobilise the diseased areas of the lungs without unduly reducing the functional efficiency of the remainder.

Collapse therapy is indicated in most cases in which the tuberculous disease is confined to one lung, and a prompt response is not obtained to rest and sanatorium treatment. It should be employed in all unilateral cases if there is cavitation, or if there are complications such as tuberculous laryngitis or pregnancy. In general, this treatment must be modified or not undertaken if there is (i) radiographic evidence of active disease in the opposite lung ; (ii) dyspnœa when at rest, generalised emphysema, or other evidence of a seriously diminished respiratory function.

The least severe and dangerous of the possibly effective types of collapse therapy is as a rule first attempted. Should it fail, however, the next more drastic method usually becomes desirable.

Relaxation of the lung is achieved by inducing an artificial pneumothorax, *i.e.*, introducing air into the pleural cavity. The lung is slowly and partially collapsed by periodical injections of filtered air, and the collapse is maintained by repeated " refills " for a period of three or more years. In experienced hands the dangers are not greater than those of other minor operations, and the results have been good. The treatment can be continued while the patient is engaged in active work ; complete arrest of the disease has been obtained in many cases in which the ordinary constitutional treatment had failed. Satisfactory results, however, must not be anticipated from unilateral pneumothorax unless the method be employed only when X-ray examination shows the better lung to be still free from extensive disease. Tuberculous tracheobronchitis (which should be excluded by bronchoscopy) contra-indicates pneumothorax therapy, and " tension " cavities are more safely treated in other ways, as is acute exudative disease.

Bilateral artificial pneumothorax is sometimes employed with advantage, more especially where thin-walled cavities are present in both lungs, and where selective collapse can be obtained. By " selective " is meant comparatively complete collapse of diseased portions of the lungs with relatively little interference with the healthy areas. In practice it is found that, in the absence of adhesions, diseased areas collapse more readily than healthy lung, so that selective collapse often occurs naturally under these conditions.

The commonest cause of failure in treatment by artificial pneumothorax, whether unilateral or bilateral, is the presence of adhesions over the area in which collapse is required. In such cases the help of a surgeon should be invoked for the direct examination of these adhesions through the

thoracoscope, so that he may proceed to divide them with a cautery, if this be practicable (*vide* Plates 10 and 11). A contraselective pneumothorax is dangerous and should be abandoned forthwith.

Revocable collapse therapy is also provided by crushing the phrenic nerve. Hemidiaphragmatic paralysis which lasts about four months results, and it is suitable for some early cases with unilateral infiltration with or without early excavation. The collapse may be made permanent by evulsion of the nerve, and either measure may on occasion be usefully combined with artificial pneumothorax. The effect of phrenic paralysis is sometimes supplemented by induction of a pneumoperitoneum. Cases of acute exudative disease with excavation, lower lobe lesions, and "tension" cavities can suitably be treated in this way. The nerve may be recrushed if necessary.

When the disease is relatively quiescent, for the most part unilateral, and when extensive excavation and fibrosis are present, artificial pneumothorax or phrenic nerve paralysis are as a rule ineffective. In such cases it may be necessary selectively to collapse (by compression) the diseased area by thoracoplasty. The modern operation, which is extrapleural, involves the resection of some or all of the upper ten ribs, depending on the extent of the disease. It has been found advisable, if the lesion is extensive, to perform the resection in several stages. Regeneration of bony tissue occurs later, leaving a rigid permanently collapsed chest wall. The operation is more hazardous than the induction of a pneumothorax, and it should rarely be advised for those under twenty or over fifty. Prior to thoracoplasty, when the pleural surfaces are adherent and when an upper lobe cavity is present, suction-drainage of the cavity as described by Monaldi may improve the patient's condition, and may make possible a less extensive subsequent operation. Following thoracoplasty, physiotherapy is essential to prevent deformity. When the respiratory reserve is adequate artificial pneumothorax for a more acute lesion on the opposite side may be combined with thoracoplasty. The operations of apicolysis and extrapleural pneumothorax have been for the most part abandoned. Lobectomy or pneumonectomy are as yet in the research stage in the treatment of pulmonary tuberculosis.

Specific Treatment.—Tuberculin has as yet proved to be ineffective and dangerous in the treatment of pulmonary tuberculosis. A preparation of living but avirulent tubercle bacilli, known as B.C.G., has been successfully used on the Continent and in the U.S.A. for the prophylactic immunisation of infants, children, and previously uninfected young adults.

Chemotherapy.—Penicillin, unfortunately, has not been found helpful in the treatment of tuberculosis. Gold preparations have been almost entirely abandoned. It would seem that little can be expected from the sulphonamide group of drugs, but research recently in the United States has shown that promin (diaminodiphenylsulphone) is of value, particularly in the treatment of tuberculous sinuses and fistulæ. It is, however, relatively toxic. In the same country and very recently streptomycin, a product of one of the actinomyces, has *in vitro* and in animal experiments proved to be a most successful antibiotic. It is now the subject of clinical research, and seems likely to be of particular value in cases with tuberculous tracheobronchitis and in miliary tuberculosis.

Heliotherapy.—Exposure of the body to sunlight or ultra-violet light, since it tends to cause exacerbation of the disease, is harmful in cases of pulmonary tuberculosis.

Village Settlements.—Patients with apparently arrested or relatively inactive chronic disease, who are capable of modified work under medical supervision, may retain their health longer under the conditions obtaining in a village settlement, such as Papworth. The psychology of the patient is of importance in the selection of those suitable for this life, and as a method of treatment it has the advantage of reducing the source from which the general population becomes infected.

Treatment of Symptoms.—*Cough.*—If coughing produces expectoration it must not be discouraged ; but a dry, unproductive cough is harmful, and the patient must be taught to control it. If sleep is interfered with, the cough may be reduced at night by an occasional teaspoonful of syrup of codeine.

Expectoration.—Profuse expectoration is largely due to secondary infections. These may be diminished by inhalations of turpentine and steam and by the regular emptying out of cavities in the lungs by postural exercises.

Hæmoptysis.—An initial hæmoptysis is seldom immediately dangerous to life, though it may cause broncho-pneumonic extension of the disease, and in every case it is alarming to the patient. It is essential that he should be reassured and kept quiet. If the bleeding is profuse, the patient should be laid supine wherever he may happen to be and $\frac{1}{4}$ gr. of morphia should be injected at once. Larger doses of morphia are dangerous on account of its action in abolishing the cough reflex. The inhalation of the vapour from a capsule containing 5 minims of amyl nitrite may check the hæmoptysis. A blood transfusion given by the drip method is sometimes of value later and effective coughing is promoted if the patient is nursed in the Fowler position.

Only rarely is it justified or indeed possible to arrest severe hæmoptysis by the induction of an artificial pneumothorax. Needless to say, this should only be attempted when it is tolerably certain in which lung the bleeding is taking place.

Slight hæmoptysis, or mere staining of the sputum, calls for no special treatment. It may be evidence of increased activity and so indicate the need for rest in bed.

Treatment of Advanced Phthisis.—In advanced cases treatment is designed to make life as tolerable as possible ; and as cure is hardly to be hoped for, restrictions are relaxed except such as prevent dissemination of infection to others. The patient is allowed up and about, even though pyrexial. Many of his symptoms may be due to secondary infections in the lungs and resulting bronchitis. These render him intolerant of cold and exposure, so that an indoor life becomes desirable. The usual treatment for bronchitis should be employed—steam inhalations and a warm atmosphere during the acute exacerbations, while alkaline expectorants, codeine, and, if necessary, morphia may be used to relieve cough and ensure rest. On no account should such a patient be sent to a mountain resort, for this will only add dyspnœa to his other troubles. Treatment of complications such as laryngeal and intestinal ulceration is dealt with in the sections devoted to these lesions.

TUBERCULOSIS OF THE PLEURA

The pleura is involved in all cases of pulmonary tuberculosis. Changes of varying extent are found at autopsy, even if there have been no clinical manifestations of pleurisy. If pleurisy occurs in a patient with other evidence

of phthisis its true nature is easily recognised ; when, however, the lungs *are apparently healthy*, a diagnosis of " idiopathic pleurisy " is often made. There can be no doubt that the majority of these cases are tuberculous. In the absence of bronchiectasis, heart disease, and nephritis, recurrent attacks of dry pleurisy, or a single attack persisting for two or more weeks, must be regarded as significant of pulmonary tuberculosis.

Pleurisy with effusion occurs most commonly in adolescents and young adults, and only rarely in young children or the aged. Males are more frequently affected than females.

A majority of cases of pleurisy with effusion are tuberculous and occur within a year of primary infection when the underlying lung is apparently normal to radiological examination. Occasionally it complicates demonstrable adult type pulmonary tuberculosis. Exposure to cold, overwork, and under-nourishment are precipitating factors.

Pathology and Morbid Anatomy.—The pleural surfaces, first the visceral and then the parietal, lose their lustre and become dull and congested. A fibrinous exudate is formed, and in course of time this becomes organised and replaced by fibrous tissue which binds the surfaces together. Similar adhesions are found between the lobes of lungs affected by tuberculosis. They are often dense and firm over the posterior aspect of the apex, and more slender and band-like over the front of the upper lobe at the level of the third, fourth, and fifth ribs. Sometimes the entire pleural cavity is obliterated, and the lung so firmly attached to the chest wall that it cannot be removed without tearing. A localised patch may be much thickened and calcified, forming a calcareous plaque.

In some cases a variable quantity of fluid exudate is poured out, and the condition becomes one of pleurisy with effusion. The exudate is usually serofibrinous, of a clear yellow or slightly greenish tinge, containing flocculi of coagulated fibrin ; occasionally it is blood-stained. Usually in tuberculous effusions the majority of the cells are small lymphocytes, but in the early stages a preponderance of polymorphonuclear cells may be found. Effusions which are absorbing frequently contain high proportions of eosinophils. Tubercle bacilli are sometimes found by direct examination, after centrifugalising the fluid, but culture or injection into a guinea-pig will usually demonstrate their presence.

Sometimes the fluid rapidly becomes turbid and purulent and a tuberculous empyema results. The latter, however, is more often a complication of established phthisis. In many such cases examination of the sediment shows it to consist of structureless debris. Tubercle bacilli are usually present, while secondary infection is not uncommon.

Dry Pleurisy

Symptoms and Signs.—Pleurisy accompanying active phthisis may cause no symptoms whatever, but as a rule there is a feeling of chilliness with sudden rise in the temperature and pulse-rate, followed by more or less dyspnœa and pain. The severity of the pain varies with the situation of the pleurisy. If it is at the apex there will be little more than a dull ache ; but if it is over the more mobile portions of the lung such as the axillary or diaphragmatic surfaces it may be agonising, and it is always aggravated by cough or deep inspiration.

The characteristic physical sign is the friction sound or rub caused by the movement of the roughened surfaces over one another with respiration. The sound varies from a leathery creak to a fine crepitation, and the latter may be distinguished from sounds arising in the lung only by the observation that friction accompanies expiration as well as inspiration. A rub may sometimes be palpable.

In diaphragmatic pleurisy no friction is heard. The central portions of the diaphragm are innervated by the phrenic, and pleurisy of this part causes pain which is referred to the root of the neck and shoulder. The peripheral portions of the diaphragm are supplied by the lower six intercostal nerves, so that in this case pain is referred to the abdominal wall, and may simulate appendicitis, inflammation of the gall-bladder, or other conditions calling for laparotomy.

Course.—After a few days the pain subsides, though it may recur in a mild form for years, especially during sudden changes of weather. The fever and cough abate after one or two weeks, but the friction sound may persist for months. Further attacks are common.

Treatment.—If the pain is severe the affected side must be strapped in such a way as to render it as nearly as possible immobile. Injections of morphia may also be necessary. In less distressing cases it will be sufficient to use counter-irritants ; the skin may be painted with tincture of iodine, or a warm cataplasm such as antiphlogistine may be applied. Cough should be restrained by occasional doses of the syrup of codeine. Restful convalescence after the attack and medical observation, including radiological examination, subsequently are essential.

Pleurisy with Effusion

Symptoms and Signs.—In some cases the formation of the effusion is insidious, in others it is preceded by the signs and symptoms of dry pleurisy. As the fluid collects the inflamed pleural surfaces become separated and the pain and the rub disappear. Pyrexia may be continued for many weeks with dyspnœa and lassitude as the chief symptoms.

The physical signs do not differ from those found in other varieties of pleural effusion. There is a striking impairment of mobility on the affected side, and " flat " dullness to percussion in the lower part of the chest. The upper limit of the dull area reaches its highest point in the axilla, and thence slopes downwards toward the midline both in front and behind. The level is higher over the back than over the front of the chest. Over the dull area, tactile fremitus and voice sounds may be completely abolished, and the breath sounds absent or faintly tubular. The heart is displaced towards the unaffected side. If the underlying lung becomes atelectatic, bronchial breathing and ægophony may be audible posteriorly at or above the level of the hilum.

Confirmation of the presence of fluid is obtained by exploratory puncture. It is wise to infiltrate the skin, tissues of the chest wall, and the parietal pleura with 1 per cent. novocaine. The fluid removed should be examined for organisms and its cell content. The sedimentation rate typically is very high and the Mantoux reaction strongly positive.

The X-ray appearance of a pleural effusion is characteristic. The fluid forms a dense shadow at the base, obliterating the outline of the diaphragm

and obscuring the costophrenic angle. The upper border is indefinite, but can be seen to slope obliquely upwards and outwards. There is more or less displacement of the heart away from the side of the effusion.

Course and Treatment.—If the effusion is small, the fluid may absorb in a few weeks, but a larger collection may persist for months. Bilateral effusions of this type are not uncommon. As a rule the pyrexia subsides before the fluid has disappeared. The presence of the fluid is probably beneficial, and does good by immobilising a diseased lung. With large effusions, however, the heart may be displaced to a dangerous extent and sudden death may result unless the excess of fluid be withdrawn. If there is distress or cyanosis, or if the heart is displaced more than 2 in., some of the fluid should be withdrawn in amounts determined by the relief experienced by the patient. Not more than a pint should be withdrawn at a time. Should radiological examination at this stage reveal an underlying tuberculous lesion it may (very rarely) be advisable to replace the fluid removed by air, and subsequently to continue the artificial pneumothorax. The routine air replacement of pleural effusions is not advised. In order to prevent undue fibrosis it is often wise to aspirate effusions which have persisted for more than six weeks.

Even if there is no sign of disease in the lung itself, the case must be regarded as tuberculous, and a prolonged course of rest, convalescence, or preferably sanatorium treatment advised. The patient should not be allowed to resume work for at least six months. X-ray examinations at no longer than three-monthly intervals are thereafter essential, and should be continued for at least three years. Only in this way is the development of a pulmonary lesion likely to be detected in its early stages.

Tuberculous Empyema.—If the amount of fluid is insufficient to cause dyspnœa by its bulk, or if the virulence of the infection is insufficient to bring about severe toxæmic symptoms, the empyema may be left alone. In the presence, however, of either of these complications the fluid should be aspirated and replaced by air, and the pleural cavity kept dry by adequate repeated aspiration. The toxæmia may be diminished by instituting pleural washouts, at the time of aspiration, with an antiseptic such as Dakin's solution. This should not be undertaken if a bronchopleural fistula is present. In secondarily infected cases, if the pyogenic organisms are sensitive, local and systemic penicillin in full doses may usefully be combined either with aspiration, or pleural washout, or as a preliminary to surgical therapy. Since there is a tendency in these cases for sinuses to form along the tracks of insertion of the needles, it is as well from the beginning to abstain from the use of local anæsthesia and to keep clear of the area of chest wall needed for thoracoplasty incision. Sinuses which develop should be treated with promin dressings. Re-expansion of the underlying lung may be promoted by closed drainage and suction. By far the greatest improvement will result (in those cases where the contralateral lung is free from active disease) from an extensive thoracoplasty on the affected side. The prognosis is, however, extremely grave whatever the treatment.

LARYNGEAL TUBERCULOSIS

Ætiology.—This is a common complication of pulmonary tuberculosis, occurring in from 10 to 15 per cent. of sanatorium patients. Primary tuber-

culosis of the larynx is exceedingly rare, and pulmonary tuberculosis almost invariably precedes laryngeal disease. Misconceptions arise because the laryngeal lesion may arrest attention before signs of pulmonary disease become obvious. Radiological examination of the lungs is essential in every suspected case. Laryngeal tuberculosis occurs in men more than twice as frequently as in women.

Morbid Appearances.—Tubercles form in the mucous membrane, giving rise to œdema and later to ulceration. The disease may only attack the vocal cords, causing thickening and ulceration of one or both cords, commonly in the posterior half. In nearly every case there is swelling of the mucous membrane on the arytenoids, and thickening of the posterior commissure which runs between them. Sometimes the epiglottis is chiefly affected, producing considerable swelling of this structure together with the mucous membrane covering the arytenoids and the ary-epiglottidean folds.

Symptoms.—When the disease attacks the epiglottis and entrance of the larynx, pain is the predominant symptom. It may be dreadfully severe and, being provoked by the act of swallowing, may lead to rapid emaciation, as the unfortunate patient will not take food. Where the lesions are limited to the vocal cords and arytenoids, pain may be absent, the symptoms being cough, hoarseness, or complete aphonia.

Prognosis.—The outlook in phthisis is rendered more gloomy by the occurrence of tuberculous laryngitis, but it is by no means hopeless.

Treatment.—Every effort must be made to deal adequately with the disease in the lungs, as this is the controlling factor. For the laryngitis, the first step is to enforce complete silence, the patient making all communications by writing or by signs, and it may be necessary to persist with this measure for many months. Local treatment includes cauterisation in selected cases where granulations are abundant. Apart from these measures therapy is largely symptomatic. Inhalations of oil of cinnamon and creosote on a Burney-Yeo inhaler may alleviate the cough ; while severe dysphagia should be treated by spraying the larynx just before each meal with a 5 per cent. solution of cocaine, or by insufflation of benzocaine (anæsthesin) through a Leduc's tube. In intractable advanced cases, alcohol injection of the superior laryngeal nerves may be desirable.

W. D. W. Brooks.

TUBERCULOSIS OF THE ALIMENTARY TRACT

Tongue.—Tuberculous ulceration occasionally occurs, nearly always secondary to advanced pulmonary disease. The edge or tip of the tongue are the parts most often involved. There is little induration and no enlargement of lymphatic glands, but the lesion may be exceedingly painful and produce dysphagia.

Pharynx.—During the terminal stages of phthisis, tuberculous ulceration of the larynx and epiglottis may extend to the pharyngeal wall and mouth.

Intestines.—Tuberculous ulceration of the ileum and colon is very common in advanced pulmonary tuberculosis, due to the swallowing of tubercle bacilli. It is found at autopsy in about 50 per cent. of patients dying of phthisis. Much less frequently it may occur as an apparently primary condition and is then often associated with tuberculosis of mesenteric glands.

Pathology.—Tuberculous ulcers of the ileum originate in the Peyer's patches and the solitary follicles; spreading round the lymphatic vessels they become transverse and may encircle the intestine. The edges of the ulcers are irregular, and the overlying peritoneum is studded with miliary tubercles. Perforation very rarely occurs owing to the tendency for adhesions to form. The latter may produce intestinal obstruction, or cicatricial contraction of healing ulcers may narrow the lumen of the intestine. The ulcers are multiple and most numerous towards the lower end of the ileum. *Fistula in ano* is tuberculous in a small proportion of cases. In all cases of fistula, an X-ray of the chest is essential.

Symptoms.—Until the ulceration becomes widespread there may be little direct indication of intestinal involvement. Later there is a troublesome diarrhœa with loose watery stools without the presence of blood or mucus. As a rule, abdominal pain and tenderness are not prominent.

Diagnosis.—The discovery of tubercle bacilli in the fæces does not necessarily indicate ulceration of the intestine. Ulcerated areas of the colon are hyper-irritable, and an X-ray examination may show persistent rapid emptying of the affected part of the gut.

Treatment.—When the condition is advanced the outlook is hopeless, and only palliative measures are possible. In earlier stages the treatment is on similar lines to that of tuberculosis in other organs.

Hypertrophic Tuberculosis of the Cæcum.—This type of intestinal tuberculosis is extremely rare, and, unlike ordinary tuberculous ulceration of the intestine, tends to occur unassociated with tuberculosis elsewhere. The disease involves the cæcum, the ileo-cæcal sphincter, and the terminal coil of the ileum, and there is often enlargement and caseation of the neighbouring glands. The lumen of the bowel becomes much narrowed by infiltration of its wall, and obstructive symptoms may occur. A mass is palpable in the right iliac fossa, which may be mistaken for a growth. Exploration is nearly always necessary to elucidate the diagnosis, and excision is often very successful. Most of the cases diagnosed as hypertrophic tuberculosis are probably really Crohn's disease (*vide* p. 327).

J. J. Conybeare.

TUBERCULOUS PERITONITIS

Ætiology.—Tuberculous peritonitis is seen chiefly in children and in young adults, though it may occur at any age. Patients with cirrhosis of the liver sometimes develop the condition. The route of infection is often doubtful but usually tuberculous lesions can be found elsewhere in the body. Infection probably reaches the peritoneum by way of the lymphatics or the blood stream. The hæmatogenous origin accounts for the generalised miliary type, and the lymphogenous for the localising form of tuberculous peritonitis.

Symptoms.—There are three main clinical types of the chronic disease: (i) the ascitic, (ii) the caseous or loculated, and (iii) the fibroid; these types depend in part on the method of infection and in part on the resistance of the patient.

The ascitic type is common in children and adolescent girls. The exudate develops gradually, and though the abdomen may be greatly distended with fluid, the symptoms are often slight. The patient loses weight and strength

and has a mild evening fever. Susceptible animals inoculated with the ascitic fluid develop tuberculosis.

In the *loculated* type the fluid is encysted, and these collections of exudate and the masses of tubercles with surrounding fibrosis may produce palpable tumours of various sizes and shapes. The intestines become matted together. The omentum is infiltrated with tubercles and may often be felt lying transversely in the upper abdomen. Due to the interference with peristalsis there are many gastro-intestinal symptoms. Colicky pain, bouts of nausea and vomiting, and alternate obstinate constipation and diarrhœa are common. Pale, bulky stools containing unabsorbed fat are often a feature resulting from occlusion of lacteals. An evening rise of temperature, tachycardia, and wasting occur. The caseous nodules are apt to break down and become secondarily infected. Fistulæ between various portions of the intestine or through the abdominal wall, especially at the umbilicus, may ultimately develop.

The *obliterative or chronic fibroid type* is a healing process in which there is widespread formation of connective tissue and no exudate is present. The intestinal tract is bound down by dense adhesions, and obstructive symptoms and signs often result. Abdominal pain may be severe in this type and is increased on movement. The patients show much emaciation and weakness but usually there is no fever.

Diagnosis.—The ascitic type is unlikely to be confused with cirrhosis or malignant peritonitis, as it is rarely seen except in children or adolescents. A large ovarian cyst may give rise to difficulty, especially with encysted effusions in the lower abdomen. A positive Mantoux test is of value in children under five years of age, and enteric fever can be excluded by agglutination tests. The ascitic fluid in tuberculous peritonitis has a specific gravity of 1,015 or over, and contains lymphocytes and often red cells. A straight X-ray of the abdomen taken erect may show multiple fluid levels owing to partial obstruction of loops of small intestine.

Prognosis.—On the whole the chronic ascitic type does best, especially in children or young adults. The loculated caseous type has the least favourable outlook. Cases are encountered which run an extremely chronic course with pyrexia and continued ill-health over many years.

Treatment.—The usual treatment for tuberculosis should be carried out—months of rest, fresh air, an abundant mixed diet, and sunshine. Heliotherapy is often most valuable, provided there is no active lesion elsewhere. Surgery is sometimes necessary in dealing with complications such as intestinal obstruction. Repeated paracentesis may be required if large amounts of fluid are present.

The constipation may be relieved by liquid paraffin or mild laxatives. Diarrhœa, if severe, can often be controlled by opium or large doses of bismuth. Fatty stools necessitate reduction of fat in the diet, but fat-soluble vitamins should be added.

TREVOR OWEN.

RENAL TUBERCULOSIS

Very commonly in miliary tuberculosis and in chronic phthisis the kidneys are found to be the site of miliary tubercles or tuberculous nodules. These, however, have no clinical significance. True renal tuberculosis arises in three

ways: (i) through the blood stream, (ii) ascending infection from tuberculous lesions in the urinary and genital organs via the periureteral lymphatics, and rarely (iii) from direct extension from neighbouring organs. Renal tuberculosis is probably always secondary to a primary lesion elsewhere in the body, and infection via the blood stream is the most common mode of spread to the kidneys. Males are more frequently affected than females in the proportion of 3 to 1, and most cases occur between the ages of twenty and thirty years, though it may be met with at all ages. Both kidneys may ultimately become involved, though usually one is affected before the other.

Pathology.—The lesions in the kidneys resemble tuberculous lesions in other parts of the body and consist of tubercles which coalesce and then caseate. In the earliest stage the disease is seen to begin at the base of the pyramids, spreading thence to involve the calices. The upper pole of the kidney is usually first affected, but the process may also begin in the lower pole. Caseation and ulceration may lead to abscess formation, the contents of which may be discharged into the pelvis and the whole kidney may thus become converted into a collection of infected cysts. The ureters are generally thickened and ulcerated, and the bladder, vesiculæ seminales, and testes are often infected.

Symptoms.—The cardinal symptoms of renal tuberculosis are: (i) frequency, (ii) pain, and (iii) pyuria. Frequency is generally the earliest and most constant symptom and its importance as an aid to diagnosis cannot be overemphasised. It may occur even before the bladder becomes involved and may be mistaken for cystitis. Pain in the form of a constant dull ache in the loin is also an important and early symptom. It is worse at night and is not relieved by rest or posture. Severe pain resembling that of renal colic occurs at times with the passage of clots of inspissated pus and debris down the ureter. Hæmaturia is not a conspicuous symptom in most cases, but it may be the first sign of the disease, and in a mild grade is present at some stage in the course of most cases. Pyrexia, wasting, anorexia, anæmia, and night sweats all occur. In many cases secondary invasion of the bladder leads to symptoms of cystitis which overshadow those due to the renal disease. Tenderness and a palpable mass in the loin usually denote a pyonephrosis. In the early stages the urine is abundant, of low specific gravity, and acid in reaction. The amount of pus present varies from a few cells to large quantities which settle at the bottom of the specimen glass as a white layer. Tubercle bacilli are frequently present, but often careful and repeated searches are necessary for their detection, which is best effected in a twenty-four hours' specimen. It is usually wise to confirm the diagnosis by growth on special media or inoculation of guinea-pigs. Tuberculous bacilluria without renal tuberculosis has been reported. Renal tuberculosis rarely heals, and treatment consists essentially in the removal of the kidney and ureter before the opposite side becomes involved. Early diagnosis, therefore, is of the utmost importance.

Diagnosis.—The diagnosis has to be made from other conditions which cause frequency, pain, pyuria and hæmaturia, such as nephrolithiasis, cystitis, pyelitis, pyonephrosis, vertebral disease, enuresis, nephritis, essential hæmaturia, and malignant disease. The discovery of a tuberculous lesion elsewhere, either in the lungs or the lower genito-urinary tract, is of significance. Cystoscopic examination should never be omitted, as the finding of

the characteristic puckering and retraction of the ureteric orifice on the affected side is diagnostic. Since a positive diagnosis usually leads to removal of the affected kidney and ureter, it is important that the renal function of the unaffected kidney be carefully estimated.

Treatment.—When one kidney has been removed for tuberculous disease much may be done to prevent the remaining organ from becoming involved. Plenty of fresh air, good food, and *adequate rest* are essential. The mode of life should be that prescribed for quiescent cases of pulmonary tuberculosis. In inoperable cases with much pain and incessant frequency it is not generally recognised that strict and absolute rest in bed of the type enforced in active pulmonary tuberculosis will often give prolonged relief from intolerable distress. Tuberculin is often prescribed in renal tuberculosis but its value has not been proved.

A. A. Osman.

TUBERCULOUS DISEASES OF THE SKIN

This large and important group is naturally divided into two parts : the first is concerned with diseases caused by the multiplication of tubercle bacilli in the skin, the second with a series of exanthematous eruptions which are an expression of active tuberculous disease elsewhere.

The first group, progressive tuberculosis of the skin, includes five conditions : (i) the primary complex ; (ii) tuberculous ulceration of the skin ; (iii) tuberculosis colliquativa ; (iv) tuberculosis verrucosis cutis ; (v) lupus vulgaris.

Progressive Tuberculosis of the Skin

The Primary Complex in the Skin.—This is seen only in those who have not been previously infected with tuberculosis ; naturally it occurs most often in children, though not always.

The initial lesion is a papule or small nodule which quickly becomes dimpled or ulcerated owing to necrosis in its centre ; it bears quite a close resemblance to a syphilitic chancre, and it is always accompanied by regional adenitis ; sometimes the regional gland becomes grossly enlarged within a few weeks, and it often eventually breaks down. This phase is sometimes accompanied by erythema nodosum.

In the course of months the primary sore either disappears spontaneously or it becomes a small patch of lupus vulgaris. There is not, however, the tendency to peripheral extension that is usual in lupus, and spontaneous resolution, both of the sore and of the adenitis, is not uncommon.

Tuberculous Ulceration (*Tuberculosis Cutis Orificialis*).—This condition is met with only in those with rapidly advancing internal tuberculosis, especially phthisis, and as an extension of this process. It is most often situated on the lips, but sometimes about the anus and genital organs. It begins in the form of miliary tubercles which rapidly undergo caseation and ulceration. The ulcer is soft and is usually covered with a crust which, when removed, reveals a reddish yellow floor exuding thin seropurulent matter. As a rule there is little pain. There is gradual extension with little tendency to healing.

Tuberculosis Colliquativa (*Tuberculous gumma*).—These rather uncommon lesions begin as sluggish hypodermic nodes which become adherent to the

skin within a few days and develop a deep red or reddish purple tint ; softening commences in the superficial part of the lesion, which generally breaks down within two or three weeks and evacuates serous or seropurulent matter, often intermingled with blood. This may continue to discharge for weeks or months, either through one or several fistulous openings, or an open ulcer may be formed with an irregular undermined margin. Spontaneous cure is, however, usual, and it is not uncommon to find the scars of old lesions, often adherent to underlying tissues. Tuberculous gummata are most often found over prominences such as wrists, knuckles, malleoli, the forehead and scalp, but they may occur anywhere. They sometimes arise as a direct extension from underlying disease of bones, joints, or lymph glands. They are seen chiefly in infants, young children, or adolescents, and are always an expression of tuberculosis elsewhere.

Diagnosis.—The lesions are often mistaken for furuncular abscesses and sometimes for tertiary syphilis, but their indolent course, bluish tint, characteristic type of ulceration, or fistulous openings and tracts, together with the fact that underlying bone or joint tissue may be affected in connection with one or more of them, serves to simplify the diagnosis. Tubercle bacilli can often be found by culture or direct examination of material withdrawn from an unbroken abscess. On the face in infants they are sometimes, on account of their bluish colour, mistaken for cavernous nævi.

Tuberculosis Verrucosis Cutis.—Generally situated on the hand, fingers, or thumb, with a predilection for the radial margin, occasionally about the anus, the initial lesion is an indolent nodule or a pustule which will not heal and which becomes transformed gradually into a granuloma surmounted by wart-like excrescences. It tends to spread centrifugally, undergoing partial healing in the centre with scarring of variable density.

The cause is direct inoculation of the infection into the skin, sometimes from an external source as in butchers or post-mortem attendants (anatomical wart). In such cases the initial lesion may be followed early by lymphangitis and tuberculous adenitis of regional glands. But warty tuberculosis of the skin is most often seen in patients suffering from chronic pulmonary tuberculosis in whom the infection has been implanted on the hand or wrist from the mouth.

Lupus Vulgaris

Lupus vulgaris is the name given to a variety of tuberculous infections of the skin of which the characteristic lesion is a small nodule known as a lupoma. This lesion may vary in size from that of a pin-head to a lentil. It is nearly flat or moderately raised above the surface and reddish brown in colour. Under glass pressure it appears as a brownish yellow opalescent spot resembling apple jelly. The disease is gradually progressive, peripheral extension taking place by the formation of fresh nodules.

Clinical Characteristics.—Lupus is far more often seen on the face, neck, and ears than elsewhere, but occurs also on the trunk, particularly the upper part, the buttocks, and the limbs. It is rarely seen on the genitalia or on the scalp. The tendency is towards a gradual centrifugal spread of the process by the formation of fresh nodules, accompanied sometimes by ulceration, while the older part of the lesion undergoes partial healing by cicatrisation. Resolution, however, is rarely complete, and active nodules are generally found in the scar tissue, a point which serves to distinguish lupus from

superficial tertiary syphilis in the scars of which active disease is practically always absent.

There are several clinical types of lupus for which the following descriptive terms may be employed :

Agminate Lupus.—This is the common type in which the lesion consists of a number of more or less closely aggregated lupomas, spreading outwards and accompanied by central rather dense scarring.

Ulcerative and Mutilating Lupus.—Ulceration and destruction of underlying tissue such as the cartilage of the nose, and mutilation of other affected parts are the special features of this variety. The progress of this destructive type may be moderately rapid.

Scrofulodermia.—Both the scars of excision, particularly when these are keloidal, and those of sinuses resulting from tuberculous glands are frequently the site of lupus.

Elephantiasic Lupus.—The lymphatics of the lips, particularly of the upper lip or of a limb, are invaded by the process with gross resultant elephantiasis-like swelling.

Erythematoid Lupus.—This is seen most often on the cheeks and nose. The lupus is very superficial, accompanied by erythema and sometimes by scaling. There may be a close resemblance to lupus erythematosus.

The term *lupus tumidus* is used for cases in which the granuloma is raised well above the surface.

Vegetating or Fungating Lupus.—In this exuberant vegetations are the striking characteristic of the infection or of a part of it.

Lupus of Mucous Membranes.—The gums, lips, palate, buccal mucosa, pharynx, and nose may be attacked. On the gums the lesions consist of exuberant bud-like vegetations ; elsewhere aggregation of vegetations may produce a mammillated or, by cicatrisation, a reticular appearance ; the lesion may ulcerate in parts. Perforation of the nasal septum is common. Blockage of a lachrymal duct is revealed by epiphora.

Lupus of the Conjunctiva.—In this situation lupus is fortunately rare. A red granular change is the characteristic appearance, with a tendency to adhesions. The cornea is generally not affected.

Ætiology.—Lupus occurs more commonly in temperate and cold countries than in warm sunny climates. It is rarely seen in the Southern Hemisphere and is relatively uncommon in North America. It is met with at all ages, but it begins far more often in childhood and adolescence than in adult life. Poverty, defective nutrition, and hygiene are common factors. The skin may be infected by external contact, but far more often by the lymphatic route from a mucous membrane, especially of the nose, and from contiguous or neighbouring tuberculous glands, especially from underlying tenosynovitis or disease of bone. When established in the skin the infection spreads by the lymphatics, fresh nodules appearing usually in the immediate neighbourhood of the early sites, but sometimes in addition at some distance away from the main mass, separated from it by an area of apparently normal skin.

In the type known as disseminate lupus the infection is blood borne. Lupus is usually unassociated with demonstrable tuberculous change in remote organs, but a quiescent pulmonary focus of infection may be present and the patient may die ultimately of pulmonary tuberculosis. In the disseminate type an internal focus must be present though it often cannot be detected. Where there is demonstrable tuberculosis of tissues other than those

in the immediate neighbourhood of the cutaneous infection, it is usually found in bone or joints.

In young children in whom the skin may be infected by contact with the floor, lupus is found on the buttocks or a lower limb with some frequency. In the latter situation advice is often sought on account of suppurative tuberculous glands in the inguinal region, the cutaneous lesion, which may be quite small, having been overlooked.

Evolution and Complications.—Untreated lupus persists indefinitely. Its rate of extension varies but is generally very slow. It is never directly the cause of death, but pulmonary tuberculosis may occur as a terminal event. Ectropion is a relatively common result of extensive lupus of the face ; it may be followed by keratitis and dense opacity.

Of the complications of lupus, epithelioma, either basal or squamous cell, more often the latter, is the most important. It has occurred most often but by no means invariably in patients who, in the past, have been treated by X-rays.

Cutaneous horns occur, sometimes in numbers, on the face and neck, in the scars of a few cases.

Treatment.—Until recently general treatment had consisted of the maintenance of a high level of nutrition supplemented by cod-liver oil and combined when possible with heliotherapy or carbon arc lamp baths. The common factor in such measures is a relative abundance of vitamin D. That vitamin D is in fact the principal agent of cure has been demonstrated by the striking effect of the administration of irradiated ergosterol, vitamin D_2 (calciferol), in large doses. This drug is best given by mouth in the form of dry tablets, or in solution in propylene glycol or alcohol. In the United Kingdom and in America it is usually measured in international units, 1 mg. of calciferol being equivalent to 40,000 i.u. The effective dose for an adult is generally about 150,000 i.u. daily for the first two to three months, followed by about 100,000 i.u. daily in succeeding months, for six months to one year. In children, 100,000 i.u. daily may be given in the initial weeks. The effect of the drug in lupus is to produce after a variable period, and sometimes after a temporary accentuation of the inflammatory aspect of the disease, a progressive flattening of the lupus nodules, and in some cases their ultimate disappearance.

Tolerance varies, some patients being able to take a larger initial dose of vitamin D than that usually prescribed, while others show signs of intolerance to the drug almost immediately. The symptoms of intoxication most often met with are nausea, epigastric discomfort, depression, fatigue, polydipsia and polyuria, and constipation ; they call for temporary cessation of treatment or reduction in dosage. The serum calcium is generally raised, and there may also be some temporary impairment of renal efficiency during the course of treatment ; in both respects, however, there are great individual variations.

Local Treatment.—Somewhat less than half of the cases of lupus may be expected to clear up under treatment with vitamin D without the help of local treatment. For the remainder local measures are necessary ; these, however, need not be instituted until the disease has been brought well under control. The following may then be adopted :

Finsen Therapy.—Light from a carbon arc is focused through a series of telescopic lenses made of quartz on to a water-cooled quartz compressor, which is held in position on a small area of skin to be treated for a period of

thirty minutes to two hours. Light so applied has a selectively destructive action on lupus nodules. The cosmetic result is excellent.

Selective caustics are of considerable value in the treatment of refractory lupus nodules. Of these the best known is liquid acid nitrate of mercury, which may be either pricked into the nodules with a pointed match stick or painted on to them.

The less well-known picric brass paste (*vide* therapeutic index, p. 844), applied under zinc strapping and removed after twenty-four to forty-eight hours, has the effect of eating into the nodules as it oxidises, leaving normal skin undamaged.

Electrocoagulation.—Lupus inside the nose, mouth, and pharynx may be treated by diathermy. This type of local treatment is sometimes used also for resistant lupomas of the skin.

Curettage.—Fungating lesions are relatively resistant to treatment with vitamin D and are best dealt with by scraping thoroughly under general anæsthesia.

Surgical Treatment.—The surgical treatment of lupus is concerned mainly with the repair of the destructive inroads of the disease on important tissues, for example, gross narrowing of the mouth or nose, destruction of the nose, blocking of the lachrymal duct and ectropion. In general, plastic surgery is contraindicated unless the patient is cured, since recurrence of lupus in grafted skin—for example, of a reconstructed nose—may prove extremely resistant to treatment.

Exanthematic Tuberculous Eruptions

These consist of—

1. Miliary tuberculosis of the skin.
2. The tuberculides.
3. Sarcoid of Bœck.

The greater number of these eruptions belong to a group named by Darier "*Tuberculides.*" They are a series of cutaneous and subcutaneous eruptions related to central tuberculosis. They differ from the progressive forms of tuberculosis of the skin in having a wider and usually symmetrical distribution, and the individual lesion has a definite tendency to spontaneous cure. They may exist in combination with easily recognisable tuberculous disease elsewhere, or the eruption may be the only obvious evidence of infection. It is probable that emboli derived from a central focus become lodged in the skin and stimulate a reaction, papule, nodule, or subcutaneous node, which results in the destruction of the bacillus. In general the tuberculides occur in those whose resistance to the infection is high, and the prognosis is usually though not invariably good.

They may be classified as follows :—

1. Lichen scrofulosorum.
2. Papulo-necrotic tuberculide, including acne scrofulosorum.
3. Miliary lupus (acne agminata, acnitis).
4. Bazin's erythema induratum.

Erythema Induratum.—Of the tuberculides, Bazin's disease is met with considerably more often than any of the other types. It is seen almost

exclusively in adolescent and young adult females with sluggish peripheral circulation. The lesions are found mainly on the posterior and outer aspects of the lower two-thirds of the legs. They begin as firm subcutaneous nodes, which in the course of a few weeks involve the skin and become red or blue in colour. Some of them soften and open on the surface, discharging thin sanious material or forming an ulcer which heals slowly ; others are absorbed. Individual lesions tend to gradual spontaneous cure, but they are succeeded by others. Cold weather aggravates the condition, but it does not disappear altogether in summer. It is sometimes accompanied by the papulo-necrotic tuberculide elsewhere, notably the fingers, hands, and elbows.

A nutritious diet, rich in vitamins, combined with carbon arc lamp or heliotherapy is the treatment of choice. Treatment by neoarsphenamine has also proved to be valuable in a number of cases. The legs should be kept as warm as possible by thick stockings and high boots lined with wool. Exceptionally a period of rest in bed is necessary.

For descriptions of other types of tuberculide, miliary tuberculosis of the skin, and sarcoid of Bœck the reader is referred to works on dermatology.

G. B. Dowling.

VENEREAL DISEASES

GONORRHŒA

GONORRHŒA is an inflammatory disease of the mucous membrane of the genito-urinary passages, due to infection by the gonococcus, which may extend locally to the genital glands and may cause systemic complications.

It is a widespread condition affecting both sexes. Although almost invariably contracted during coitus, infection from closets, articles of toilet, clothing and towels is possible and is not uncommon in female infants. The incubation period varies from three to ten days, but occasionally may be up to thirty days.

The gonococcus is a minute, gram-negative, kidney-shaped diplococcus, which is cultivated with difficulty. In recent infections the gonococci are plentiful and are found in clusters within the pus cells and in pairs scattered between the cells. Outside the tissues it dies rapidly when dried, but if moist and warm it may live for several days.

The parts affected in the male are primarily the urethra, from which the infection frequently spreads to the epididymes, prostate gland, and seminal vesicles.

In the female the initial infection involves the urethra and cervix ; later the uterus and Fallopian tubes may be affected. The vulva, lower vagina, urethra, and rectum are liable to be infected in female infants.

Treatment of gonococcal infections by penicillin and sulphonamides has for practical purposes greatly modified or abolished most of the characteristic features of the disease. The descriptions given below refer to cases untreated by modern methods.

GONORRHŒA IN THE MALE.—The initial symptom is a slight irritation or scalding during micturition, soon followed by a purulent discharge. The lips of the urinary meatus are tender, swollen, and everted. The urethral mucous membrane is œdematous, injected, and bathed in pus ; the glands of Littré and the lacunæ are infected ; periurethral swellings and abscesses may result which sometimes rupture externally on the under surface of the penis or in the perineum. Inguinal adenitis of transient duration is common, though suppuration is rare.

After several weeks, if untreated, the acute inflammation subsides, but a condition of intermittent urethral discharge, known as *gleet*, becomes established, and the urine contains yellow opaque threads which contain gonococci. This stage may last from a few weeks to many months, being usually dependent on a chronic infection of the glands of Littré or of the lacunæ—lesions which can be identified by means of a urethroscope. This chronic infection frequently results in a localised infiltration by lymphocytes of the submucous layers which, if marked, forms a soft or inflammatory stricture ; years later a hard, fibrous stricture may follow.

The infection, if untreated, often spreads to the posterior urethra in the second to the fourth week. The onset is frequently insidious, but may be acute and cause frequency of micturition with pain, slight fever, general malaise, and hæmaturia. When there is acute infection of the prostate gland a large, hot, tender swelling, in which the seminal vesicles may participate, can be felt per rectum. Some perineal pain and severe dysuria are usual, but pain on defæcation is slight. Retention of urine is a common accompaniment. True abscess formation is rare; this usually ruptures into the urethra or occasionally into the rectum with immediate relief. Gonococcal proctitis is a rare sequel to rupture of a prostatic abscess; such proctitis is usually acquired by a catamite during sodomy. When rupture is delayed malaise, toxæmia, and fever are marked; rigors are not infrequent and the condition may simulate malaria or endocarditis.

Chronic prostatitis and vesiculitis may persist for many years and are often the hidden focus of infection in cases of gonococcal arthritis or iritis. The associated urethral discharge is slight in amount and intermittent; long periods free from discharge may be followed by a relapse. On rectal examination enlargement and nodules may be recognised. The condition is frequently intractable partly on account of the inadequate drainage but chiefly because of the absence of characteristic localising signs or symptoms. In many instances the diagnosis can be made only by the detection of pus and bacteria in the prostatic secretion or semen. A urethral discharge experienced only on defæcation is suggestive of such infection. Secondary invasion with pyogenic or coliform bacteria is a constant feature. Gonococci are rarely found after the first few months.

Gonococcal epididymitis is a frequent complication; an acute tender swelling suddenly appears in the scrotum, formed chiefly by the lower pole of the epididymis. Suppuration, however, rarely occurs. Hard nodules may persist in the epididymis for months, and sterility is frequent after bilateral infection.

Treatment.—Penicillin has a marked curative effect in gonorrhœa, both in fresh and in sulphonamide-resistant infections. The standard treatment consists of 150,000 Oxford units of aqueous sodium penicillin given in three intramuscular injections, each of 50,000 units, at three-hourly intervals, or a single injection of 250,000 units of penicillin in a beeswax-oil medium may be given. In a very high proportion of cases the gonococcus disappears within twenty-four hours, although some discharge may persist for a few days longer. In the event of failure a similar course repeated a week later may be effective, or the case may respond to sulphathiazole in dozes of 1·5 gm. thrice daily for five days.

Since penicillin in this dosage is capable of healing early syphilitic lesions, it is essential to examine all cases of gonorrhœa for signs of syphilis before penicillin treatment is commenced. Since, also, penicillin given for gonorrhœa may delay the appearance of a syphilitic chancre, it is advisable to do a serological test for syphilis on treated cases of gonorrhœa at the third and sixth month after treatment.

Acute prostatitis or vesiculitis requires rest in bed with rectal douches of hot saline; pain and frequency of micturition may be relieved by 20 minims of tr. hyoscyami orally, or if severe will require rectal suppositories of morphia and atropine; kaolin poultices or lotio plumbi c̄ opio will relieve the pain in acute epididymitis.

Chronic anterior urethritis in the male may persist for many months or there may be temporary improvement followed by a relapse. In most of the refractory cases there is a chronic infection of some of the glands of Littré or a lacuna. When there is marked peri-glandular inflammation a soft stricture, which gives no signs of obstruction, frequently ensues. These are treated by repeated instrumental dilatation and irrigation of the urethra for many weeks. A peri-urethral abscess usually subsides but aspiration or, less commonly, incision may be required.

The treatment of chronic prostatitis and seminal vesiculitis consists of measures directed to improve drainage such as regular prostatic and vesicular massage, rectal diathermy, and urethrovesical irrigations with pot. permang., flavine, or mercury oxycyanide in a 1 in 8,000 solution. Sulphonamide or penicillin therapy is most useful in chronic gonorrhœa when drainage has been re-established. Penicillin should be given for at least three days.

Stringent tests are required before a case is to be considered cured. These include the absence of discharge, a clear urine, negative films, and cultures for gonococci of the urethral and prostatic fluid over a period of three months after treatment.

GONORRHŒA IN THE FEMALE.—The sites of infection in the female are the urethra, vulva, and cervix, and in most cases all these are involved. The symptoms are vaginal discharge, painful and frequent micturition, and swelling of the labia. The urinary meatus becomes red, swollen, and everted; pus can be expressed from the urethra by digital pressure along the anterior wall of the vagina. In some women the infection is mild and devoid of symptoms from the outset and remains unsuspected until a sexual partner becomes infected. Chronic urethritis is frequently due to the infection of minute ducts near the urinary meatus (Skene's ducts). Further extension of infection may lead to gonococcal cystitis and rarely pyelitis.

Acute infection of the cervix results in a swollen injected os, from which thick tenacious yellow pus issues, and the vaginal walls are bathed in pus; in the chronic stage erosions of the cervix are frequent. Bartholin's ducts and glands are frequently infected. Further extension of infection is followed by endometritis and salpingitis. Localised peritonitis of plastic type is a frequent accompaniment, but general spreading peritonitis is rare.

The rectum may be occasionally infected by the vaginal discharge, and unless giving rise to prominent symptoms, this is often overlooked. Gonococcal infection may become chronic in the urethra or cervix, producing few or no clinical signs, and may cause gonorrhœal iritis and arthritis. *Trichomonas vaginalis* infestation may coexist with gonorrhœa or may produce a similar discharge. This condition is treated by vaginal pessaries containing acetarsol. Two of these are inserted at night for seven consecutive nights. Relapses are not infrequent.

Female children, especially infants, are particularly liable to become infected from bed-clothes or towels. The infection produces a vulvo-vaginitis in which the vulva, hymen, and lower vagina are affected. In the acute stages there is much swelling, pain, and purulent discharge. The urethra and rectum are frequently infected. Extension to the uterus or Fallopian tubes and localised peritonitis are rare. Joint lesions or iritis are very rare.

Treatment.—General measures and sulphonamide therapy are similar to those for men. Penicillin is not as effective in gonorrhœa in the female as it is in the male; the injections should be continued for at least three days. In

acute vulvitis and acute endocervicitis treatment with hot sitz-baths is advisable and rest in bed essential. On account of the danger of syphilis, acquired at the same time as gonorrhœa, being masked or delayed by brief penicillin therapy, gonorrhœa during pregnancy should be treated with sulphonamides. Penicillin should be reserved for refractory infections and should not be given under five or six weeks.

Acute salpingitis which is indicated by pyrexia and pain in the lower abdomen associated with an enlarged and tender Fallopian tube is best treated by rest in bed in the Fowler position, radiant heat or hot fomentations, and frequent hot vaginal douches. The development of pyosalpinx or general peritonitis may require surgical intervention.

Tests of cure should include the gonococcal complement fixation reaction and repeated microscopic examinations and cultures of the secretions of the urethra and cervix, especially following menstruation, over a period of six months.

The vulvo-vaginitis of children is treated with sulphathiazole (1 to 2 gm. daily for four days), or by intramuscular injections of penicillin (10,000 units every three hours for twenty-four hours). Gonococcal infection in little girls is particularly intractible and repeated courses of sulphonamides or penicillin may be required.

Gonorrhœal Ophthalmia and Ophthalmia Neonatorum.—Infection of the conjunctiva is caused by the accidental transference of gonococcal pus into the eye; it also occurs during transit of the new-born infant through the infected maternal passages. The application of a 1 per cent. silver nitrate solution to the baby's eyes immediately after birth is an effective prophylactic measure.

The infected eye and eyelids become severely inflamed; the purulent discharge is copious and chemosis is severe. If untreated there is rapid ulceration of the cornea and in some cases complete destruction of the eye.

Local therapy with penicillin is remarkably effective. After wiping away the pus two drops of a solution of 10,000 units per c.c. of pure penicillin are instilled followed by one drop every minute for thirty minutes. At the end of this period pus formation may cease, but instillation should be continued six times at five-minute intervals followed by a similar number of instillations at half-hourly, one-hourly, and two-hourly intervals. The intramuscular injection of penicillin—200,000 units at three-hourly intervals for a period of nine hours—is also effective. The use of penicillin is expected to reduce considerably the number of infants blinded by gonorrhœal infection.

Metastatic Gonococcal Infection

Septicæmia is rare. When this occurs there is hectic fever, with enlargement of the spleen and purpuric rashes. Gonococci may sometimes be cultivated from the blood and the spleen. Acute bacterial endocarditis and pericarditis are almost invariably fatal.

Gonococcal iritis and irido-cyclitis occur in chronic gonorrhœa and are usually associated with chronic disease of the prostate or seminal vesicles in the male, and cervicitis or salpingitis in the female. Both eyes tend to be affected successively, and recurrences are frequent. Arthritis is often present in these cases.

Gonorrhœal Rheumatism.—The gonococcus shows a special tendency to attack the joints, tendon sheaths, and bursæ. This occurs during the acute or chronic stage of gonorrhœa in about 5 per cent. of untreated cases. Since the introduction of the sulphonamides and penicillin for gonorrhœa such complications have become rarities. In the chronic stage there may be no symptoms of local infection, but examination reveals a focus in the genito-urinary passages.

In acute arthritis, which rarely ensues before the third week of the disease, the onset is sudden with marked swelling of the joint chiefly affecting the peri-articular structures ; effusion into the joint cavity is usually small in amount. There is considerable constitutional disturbance and the patient is feverish and sleepless from pain and tenderness. Considerable and sometimes rapid wasting of the adjacent muscles may take place. When the swelling subsides and in the subacute variety associated with chronic gonorrhœa, the plastic inflammation involving the peri-articular structures frequently causes fibrous ankylosis. Acute arthritis is often limited to one large joint such as the knee or wrist, but cases of acute polyarthritis are met with in which several large joints are affected, together with the joints of the carpus or tarsus and interphalangeal joints. Infections of the temporo-mandibular or sterno-clavicular joints are not particularly common in gonorrhœa, but they rarely suffer acutely in any other infection. Spondylitis is occasionally of gonococcal origin.

Gonorrhœal rheumatism may be limited to fleeting joint pains without physical signs, and also occasionally causes a chronic hydrops of one large articulation, such as the knee, which may persist for many years. The tendo Achillis with its underlying bursa may become inflamed, also the plantar fascia, resulting in a painful flat foot or painful heel.

Treatment.—Attention to the local focus of disease in the genito-urinary tract is essential. Considerable benefit may follow the administration of sulphonamide compounds or penicillin ; the latter should be given to a total of 500,000 units over a period of several days.

In the acute stage when pain in the joint is marked, splints may be required, but on account of the tendency to ankylosis early movement should be encouraged. Local application of radiant heat or kaolin poultice is beneficial. In subacute arthritis, fever therapy is often followed by improvement. This may be effected by the intravenous injection of triple typhoid (T.A.B.) vaccine, 25 to 50 millions, repeated two or three hours later, or the patient may be treated with the Kettering hypertherm, in which the height and length of the fever can be controlled. In the more chronic stage the arthritis may respond to a gonococcal vaccine. Prolonged treatment by massage and exercises is essential for complete recovery.

LYMPHOGRANULOMA INGUINALE

(*Lymphopathia Venereum*)

Lymphogranuloma inguinale or Climatic bubo is a specific virus disease involving the inguinal glands and characterised by chronic suppuration with multiple sinuses. The infection, which is of venereal origin, is frequent in tropical areas but uncommon in Europe.

The transient primary lesion appears as a minute erosion or papule, usually situated in the coronary sulcus of the penis, within two weeks after coitus. Two to three weeks later a painless swelling of the inguinal glands appears in one or both groins. The rate of development of the bubo is variable.

In the earlier stages of the adenitis the overlying skin assumes a bluish-violet tint and becomes adherent to the glands; the surrounding tissues become infiltrated and hard. Multiple points of suppuration occur and discharge yellow, tenacious pus. There also may be swelling of the iliac glands. The general symptoms, which are variable, include fever, pains in the limbs, loss of weight, and prostration. Severe headache may occur with transient meningismus. The systemic symptoms last a short time, but the bubo usually forms slowly and the resultant sinuses may drain for months.

In women proctitis is frequent, and a rectal stricture may be present in long-standing cases. Elephantiasis vulvæ may follow if the lymphatic channels be extensively obstructed. The typical inguinal adenitis seen in the male is uncommon.

The intracutaneous reaction of Frei becomes positive in almost all cases of lymphogranuloma inguinale in two to three weeks and may persist for many years after recovery.

Treatment.—Excellent results in the early stages have followed the use of oral sulphadiazine or sulphapyridine. In the later stages response is slow and several courses of treatment may be needed. Good results are also given by a course of intramuscular injections of anthiomaline (lithium antimony-thiomalate) two or three times a week for three weeks. Local aspiration or partial excision of the bubo is occasionally required but is best avoided.

SYPHILIS

Syphilis, or lues, is a chronic infective disease which may affect all organs and tissues of the body, and manifestations may appear at intervals over many years, interspaced with periods of latency. Its natural occurrence is limited to the human race, but it can be transmitted experimentally to apes and rabbits.

Congenital syphilis is due to the infection of a child by the transmission of the disease from the mother during pregnancy.

The clinical course of the acquired infection has been divided into three stages which are separated by intervals. The stage of the initial lesion is known as the primary stage, that of generalised tissue reaction as secondary syphilis, and that of the later recrudescences as tertiary syphilis.

Ætiology.—Syphilis is due to infection of the tissues with the *Spirochæta pallida*, a protozoon discovered by Schaudinn and Hoffman in 1905. This organism is slender, motile, and of varying length, 5 to 25 μ, and about 0·25 μ in width. The spirals are regular, closely twisted, and vary from ten to thirty in number. Its movements of progression are slow, but those of rotation and of bending are rapid. It is destroyed by heat or absence of moisture. From the lesions of the primary and secondary stage the spirochæte is readily isolated, but in the tertiary lesions they can be found only with difficulty. In congenital syphilis they are often present in enormous numbers in the viscera, such as the liver, spleen, and suprarenals.

ACQUIRED SYPHILIS

Mode of Infection.—Infection usually occurs through some minute abrasion on the genital organs during sexual intercourse with an infected person in whom there is an active syphilitic lesion, or spirochætes may be present in the seminal fluid or vaginal secretion of infected persons. At the site of inoculation, after an interval of about a month, a lesion known as the primary chancre appears.

Contact with infective material may result in an extra-genital chancre, *e.g.*, lip, mouth, finger, or nipple. Generalised secondary syphilis, without any primary lesion, has followed blood transfusion from syphilitic donors.

The infectivity of syphilitic lesions varies considerably, being most marked in the secretion from the chancre and from the moist lesions of the secondary stage. In the tertiary lesions the infectivity is decidedly less.

PRIMARY STAGE.—The inoculation by the infecting organism is followed, after an interval usually of about a month, by the development of a chancre at the site of inoculation. The initial lesion is a minute papule which within a few days becomes eroded and gradually indurated at its base ; at the end of a week or so a typical hard chancre is present. This is a small, painless, indolent, oval or round sore with a firm button-like indurated base and sloping borders ; it is raw ham in colour and is covered with a serous discharge. Many variations from the typical hard chancre are met with, but in all of them some degree of induration is present although it is much less evident in lesions in females.

In the secretion from the deeper parts of the primary sore spirochætes are readily found on dark-ground microscopy.

Syphilitic chancres are usually solitary, but may be multiple. In men, the most common sites are the prepuce, the glans penis, and the frænum. A chancre or a soft sore may be concealed by phimosis, but the former can be felt through the œdematous prepuce. Multiple syphilitic fissures on the preputial margin are not infrequent ; these, like the uncommon meatal chancre, are usually painful.

In the female, chancres occur on the labia, which may be much swollen, on the clitoris, the urinary meatus, the fourchette, and the cervix.

Shortly after the appearance of a genital chancre the inguinal glands undergo a hard, discrete, painless enlargement. A similar enlargement of the posterior cervical, epitrochlear, and axillary glands soon follows.

The invasion of the blood stream by spirochætes takes place during the incubation period, and has already occurred before the chancre appears ; thus excision of the primary chancre cannot prevent general dissemination of the disease.

The untreated chancre gradually heals within about two months, and may leave only a minute and superficial scar. At the time of the appearance of the chancre, the Wassermann reaction is negative and remains so until two to three weeks have elapsed.

Various sores other than syphilitic chancres are met with on the genitalia. Infection with Ducrey's strepto-bacillus, resulting within a few days in one or more chancroid ulcers (soft sores), is common in tropical countries but infrequent in Britain except in seaports ; they are rare in women. Chancroid ulcers are characterised by their irregular deep ulceration, undermined edge.

sloughy floor, and tenderness. The ulcer feels soft until healing is well advanced. Although chancroid produces no constitutional effects, swelling of the inguinal glands is a common feature. The swollen glands gradually become adherent to each other and to the skin, forming a red, painful swelling in one or both groins. Syphilitic glands rarely become matted and suppuration is exceptional, whereas in the chancroid bubo both are frequent. The infection responds well to sulphadiazine and often to a vaccine of Ducrey's bacillus given intravenously, neither of which improve a syphilitic chancre.

Simple erosions in the genital area may be caused by balanitis, scabies, or herpes genitalis. Carcinoma of the penis is often mistaken for a chancre in elderly men.

SECONDARY STAGE.—Within four to six weeks of the appearance of the primary sore the stage of general tissue reaction known as secondary syphilis becomes manifest. Constitutional disturbances such as slight fever, loss of appetite, headache, malaise, alopecia, and pains in bones and joints may occur, and anæmia may be severe.

Cutaneous Eruptions.—The main characteristics are symmetrical distribution, polymorphism, a lilac or ham colour, and lack of irritation. The types commonly met with may be classified as follows :—

1. *The Macular Eruption* is the earliest and most frequent type, consisting of small scattered discrete spots of a pale rose colour which appear at first on the flanks and later on the abdomen, back, and flexor surfaces of the unexposed parts of the limbs. On first appearance the pale rose mottling (roseolar rash) is inconspicuous and is difficult to see, especially by artificial light. In a few days the tiny macules increase in size and number and their colour deepens, and the eruption resembles that of measles ; there is, however, little or no fever. The macular rash must be distinguished from other erythemata, pityriasis rosea, and drug rashes.

2. *Papular Eruptions*, which are frequent, occur some weeks later than the macular rash. The papules, which form slowly, vary in size from a pinhead to a split-pea and are of round or oval contour and of a reddish brown colour. The spots are indurated and can be readily felt in the skin ; they persist for some weeks. Their distribution is wider than that of the macular rash, and in contrast they may be plentiful on the hands and feet, the extensor surfaces of the limbs and on the face and genitalia ; on the forehead they are often prominent and are termed the " corona veneris." In dry localities the papules become scaly and occasionally resemble psoriasis.

3. *Condylomata.*—In moist situations, such as the perineum and axillæ, the papules are more profuse in growth and become sodden ; these are known as condylomata, the moist surfaces of which are usually teeming with spirochætes. When situated near the anus they are frequently mistaken for hæmorrhoids.

4. *Rupia.*—In debilitated patients infection of some of the papules with pyogenic micro-organisms may occur, and the surface becomes covered with a dark crust under which a shallow ulcer soon forms. Dried layers of pus add to the crust, forming a limpet-shaped scab known as syphilitic rupia.

5. *Follicular Eruptions.*—These occur around the hair follicles and sebaceous glands, and may simulate acne vulgaris ; they frequently become pustular.

In some patients, especially women, the rashes may be absent, or transient eruptions may occur which either are not noticed or are not

remembered by the patient. The Wassermann reaction, however, is strongly positive.

Mucous Membranes.—A bright erythema of the palate and fauces is met with early in the secondary stage. Later, superficial lesions occur frequently on the fauces, tonsils, or inner surface of the lips. They constitute small, oval, or reniform erosions, with a pearly grey centre and a thin red margin (*mucous patches*). These lesions are soft, smooth, and painless, and are usually of transient duration; they may, however, persist, broaden, and develop a slimy appearance, and are termed *snail-track ulcers*; their secretion, like that of the erosions, contains many spirochætes and are highly infective. When situated on the tonsil or wall of the pharynx they tend to ulcerate. This condition may simulate faucial diphtheria or, when ulceration ensues, may be mistaken for Vincent's angina; there is, however, no unpleasant odour. The husky voice, characteristic of the secondary stage, is due to the presence of erosions in the larynx.

Other syphilitic manifestations in this stage are infrequent. Jaundice, with a tender enlarged liver, is sometimes seen and may rarely progress rapidly to a fatal acute liver atrophy. The spleen also may be enlarged. The kidneys are rarely affected, but gross albuminuria with few renal casts occasionally occurs, which responds readily to specific treatment. Iritis of plastic type may occur but relapse is infrequent. The effects of secondary syphilis on the meninges and nervous system are discussed on page 635.

Following the decline of the florid secondary stage there ensues a period of apparent quiescence termed "latent syphilis," which may vary in duration until tertiary manifestations appear, from two to over twenty years. The Wassermann reaction is usually positive throughout. During the first few years mucosal or cutaneous lesions may recur. These relapses, which lack the widespread distribution of the earlier secondary manifestation, tend to be isolated, more infiltrated, and of longer duration, *e.g.*, faucial ulceration, rupia, and condylomata. A prolonged latency is a prominent feature of syphilis in women, particularly during the child-bearing period; the offspring, however, are frequently infected.

TERTIARY STAGE.—Tertiary lesions are to some extent determined by such factors as intercurrent disease, prolonged physical strain, trauma, and age. They tend to be asymmetrical, isolated, and extensive, and limited to a particular tissue or organ; ulceration is frequent; although, unlike the secondary syphilitic lesions, there is little tendency to natural resolution, response to treatment is rapid.

Pathology.—The tissues affected by tertiary syphilis become gradually infiltrated with granulation tissue containing plasma cells and lymphocytes; the smaller blood vessels are affected by endarteritis obliterans of gradual progression which renders the area relatively avascular; this results in slow necrosis of the central portion of the affected area with subsequent ulceration.

Such an aggregation of syphilitic granulation tissue is known as a *gumma*; frequently this forms a moderate-sized, painless, circumscribed swelling of firm consistence and indefinite margins. Such gummata displace or replace normal tissues, affect surrounding structures by pressure, and when ulcerated, quickly become infected with pyogenic organisms.

In situations which are protected from injury or irritation, gummata of long standing may become encapsuled by thick fibrous tissue, and remain thus for a long period. When situated in cutaneous structures or in superficial

bones, necrosis occurs early and produces a circular punched-out ulcer containing a sloughy mass similar in appearance to wet wash-leather. On healing they present thin, circular silvery scars, often with a brown pigmented border, especially on the front of the legs where they are of frequent occurrence. The lumbar, gluteal, and scapular regions are also often affected. Tertiary syphilides also occur as isolated areas, sometimes very extensive, of diffuse gummatous infiltration of the skin with peripheral groups of reddish brown nodules. Later the nodules fuse and degenerate into irregular areas of indolent ulceration which tends to heal in the centre whilst it slowly spreads at the margin. When situated on the face there is some resemblance to lupus vulgaris, but in syphilis the progress is more rapid.

Gummata, diffuse or localised, of mucous membranes rapidly necrose, causing extensive ulceration in the nose, palate, pharynx, or larynx.

Late Syphilis of Bone and Joints.—Syphilitic periostitis and osteomyelitis give rise to the formation of a diffuse gummatous infiltration or of isolated tender nodes. The bone becomes rarefied, and around this there is a zone of bony sclerosis. The breaking down of this gummatous material results in the slow disintegration of bone—a condition termed *syphilitic caries*.

Syphilitic infection is frequent in the flat bones, such as those of the skull, the palate, the nasal bones, the nasal septum, the sternum, and clavicle, with subsequent ulceration and pyogenic infection. Among the long bones syphilis has a predilection for the tibia, less frequently the bones of the forearm or femur ; the shaft of the bone is usually involved, rarely the epiphysis.

The joints are rarely affected in the tertiary stage of the disease. Gummatous disease of a joint involves chiefly either the synovial membrane—*gummatous synovitis*—or the articular ends of the bones—*gummatous osteo-arthritis*. Charcot's joint or tabetic neuro-arthropathy is a degenerative condition not due to articular syphilitic disease (*vide* p. 645).

Visceral Syphilis.—Syphilis of the liver is described on page 348. Syphilis may affect the kidneys in the tertiary stage by producing a condition of chronic glomerulo-nephritis which responds well to antisyphilitic treatment. The testes are often affected with a diffuse gummatous orchitis producing a solid heavy enlargement devoid of sensation.

Ulceration in the rectum in women eventually forming a stricture was formerly considered to be frequently of syphilitic origin. These conditions now appear to be due chiefly to gonococcal pelvic cellulitis and proctitis, or more rarely lymphogranuloma inguinale.

Tertiary lesions are common in the mouth, especially in men. In chronic superficial glossitis, which is very frequently of syphilitic origin, the surface of the tongue presents irregular white patches. This is known as *leukoplakia*. Sometimes it is lobulated from a deeper contracting sclerosis of syphilitic origin ; between the lobules fissures develop which are often the precursors of carcinoma linguæ. Isolated gummata, which are situated more deeply, occur in the centre of the tongue and frequently ulcerate. The latter respond readily to antisyphilitic treatment but leukoplakia rarely improves.

In the palate, fauces, nasal cavity, pharynx, larynx, and œsophagus ulceration may be extensive, simulating lupus or a malignant ulcer.

Syphilis of the cardio-vascular system is described elsewhere (*vide* p. 431).

Asymptomatic Neurosyphilis.—In this phase, although there are no physical signs or symptoms of involvement of the nervous system, examina-

tion of the cerebrospinal fluid will reveal some abnormality indicative of a persistent syphilitic process. Asymptomatic neuro-syphilis may be present in the latent or tertiary stages of syphilis, and may occur with or without other syphilitic manifestations. It is a phase of considerable importance because it is the precursor of clinical neurosyphilis, and because its early recognition and treatment may prevent the onset of tabes dorsalis or general paralysis of the insane. Asymptomatic neurosyphilis should be suspected in cases whose blood Wassermann reaction remains persistently positive in spite of full treatment, in those treated cases who suffer a serological relapse, and in all cases of latent syphilis. In these cases examination of the cerebrospinal fluid, including the cell count, globulin and protein estimation, Wassermann reaction and Lange reactions, is imperative (*vide* p. 636).

This symptom-free phase may last from one to ten years or more, during which period the pathological changes in the cerebrospinal fluid are gradually progressing in degree. At first protein and cellular changes are slight in degree; the Wassermann test is negative or slightly positive, and the Lange reaction shows slight positive changes. Later both cell number and protein content show a decided increase, the Wassermann reaction becomes markedly positive, and the Lange test approaches the luetic or paretic zone.

CONGENITAL SYPHILIS

Congenital syphilis is an infection that is acquired *in utero* from the mother, usually in the later months of pregnancy, and is, strictly speaking, not an inherited disease. Owing to the nature of the attachment of the fœtus to the uterus, congenital syphilis shows no stage comparable to the primary stage of acquired syphilis but is generalised from the onset. Spirochætes are present in profusion in the liver, spleen, adrenals, lungs, and many other organs.

The syphilitic baby is usually apparently healthy at birth but within two to six weeks it begins to lose weight and becomes thin and sallow; the skin is wrinkled and sometimes of a café-au-lait colour. In the third or fourth week a muco-purulent or sanious nasal discharge appears which causes redness and excoriation of the nares, nostrils, and upper lip. The nasal obstruction is often considerable and interferes with the infant's ability to suckle. In this condition, which is termed "snuffles," the syphilitic inflammation is extensive and spreads throughout the nasal cavity and may cause necrosis of the nasal cartilages with subsequent lack of development of the nasal bones. The "saddle nose" deformity ultimately produced is one of the well-known stigmata of congenital syphilis.

Cutaneous Lesions.—Rashes are one of the commonest manifestations of congenital syphilis, occurring in 60 per cent. of cases; they appear from three to eight weeks after birth. They are protean in character and may be erythematous, macular, papular, or vesicular; of these, the scaly macular eruption is the most frequent. Their colour varies from a yellowish tinge to a coppery or raw ham tint. They may be scanty or profuse and are usually well marked on the buttocks, flexor surface of the limbs, and face. Whilst chiefly dry and scaly, they are apt to become eczematous in the napkin area. Extensive brownish red glazed areas with peeling at the edges are frequent on the palms and soles, and occasionally may be the only cutaneous lesions

present. Condylomata are frequent around the anus. The rare pemphigus eruption occurs early and may be present at birth. It consists of sero-purulent bullæ, well marked on the palms and soles, and produces a severe general reaction, often with a fatal termination. Mucous patches in the mouth or on the fauces are common.

Rhagades are fissures appearing on the margins of the lips which follow circumoral syphilitic eczema and leave permanent scarring. The larynx may be the seat of syphilitic inflammation, causing a hoarse cry.

Bone Lesions.—These are common and occur early. Pseudo-paralysis of infants is caused by an acute epiphysitis termed osteochondritis syphilitica which attacks the end of a long bone, most frequently the humerus, radius, or ulna ; it produces tender swelling of the neighbouring joint and varying degrees of loss of power in the limb. Acute or chronic periostitis of the shaft is very common at any age and may give few clinical signs. X-ray examination is a valuable method of diagnosis. Syphilitic dactylitis of the phalanges or metacarpals results in a fusiform swelling.

In the skull, hypertrophy of spongy bone at the edges of the anterior fontanelle gives rise to Parrot's nodes, a condition which, when well marked, is termed the hot-cross bun skull but is not characteristic of syphilis alone. Cranio-tabes, a parchment-like thinning of the parietal and occipital bones, is also met with in other debilitating diseases such as rickets. Both these conditions are now rarely seen.

Visceral Lesions.—In the early months of infancy there may be marked enlargement of the spleen and liver. Renal infection may be shown by the presence of blood, albumin, and casts in the urine. Paroxysmal hæmoglobinuria is frequently due to congenital syphilis. White pneumonia, usually in still-born children, is an interstitial fibrosis of the lung of syphilitic origin. The testicles in infancy may undergo bilateral painless enlargement, frequently followed by atrophy. Disseminated choroiditis may be present in infancy but is rare.

Delayed Congenital Syphilis.—If the infant survives there is a latent period between the lesions of infancy and those of later childhood comparable to the latent period in acquired syphilis, or the early manifestations of syphilis may be absent. During this interval the child may develop normally, or be stunted in growth and backward in mentality ; later, various lesions may follow.

Lesions of bones and joints are of frequent occurrence ; syphilitic periostitis is particularly common and in the tibiæ produces characteristic irregular nodes on the anterior surface of the heavy thickened and forward curved tibiæ—the sabre-blade tibia. This condition is bilateral, although the changes may be more advanced on one or other side. Periostitis gives rise to general or nodular enlargement of the clavicle, or localised swellings on sternum, skull, or bones of the forearm and leg. Dactylitis may occur later as well as in infancy. Symmetrical painless synovitis of the knee-joints, known as *Clutton's joints*, are met with about puberty ; gummatous synovitis simulating tuberculosis of a joint is less frequent.

The eyes are liable to chronic interstitial keratitis at any age up to and including adult life, but most frequently between six and sixteen years. The condition is bilateral, and usually affects one eye before the other; the cornea appears opaque, resembling ground glass, and ciliary congestion is marked. Vascularisation of the cornea gives rise to the "salmon patches." Fair

recovery usually takes place after the condition has lasted from one to two years, but relapse is frequent. Iritis, choroiditis, or retinitis may coexist, leaving permanent changes and interference with vision.

Neurosyphilitic lesions may occur in congenital infection. Juvenile tabes and general paralysis occur in adolescence, comparable to similar lesions in acquired syphilis. The cerebrospinal fluid is abnormal in from 20 to 40 per cent. of all cases of congenital syphilis. Meningo-vascular conditions also occur, and congenital syphilis is considered to be sometimes a causative factor in epilepsy, imbecility, spastic diplegia, and hydrocephalus. Nerve deafness occurs about puberty ; the condition is bilateral, and frequently complete and permanent.

Cutaneous manifestations, which resemble those of the tertiary stage in acquired syphilis, are seen in late childhood. Favourite sites are the face, especially around the nose and the mouth, and the skin over the sternum, ribs, clavicle, and front of the leg. They are chronic, frequently ulcerate, and extend slowly, healing in the centre and simulating tuberculous lesions. Ulceration of the hard and soft palate with ultimate perforation is frequent, and in the larynx may cause severe stenosis on healing.

The milk teeth frequently exhibit imperfections but none that are characteristic of congenital syphilis. The permanent teeth, however, show striking changes, especially in the upper central incisors, which are known as *Hutchinson's teeth*. There may be irregular erosions in the cutting edge or irregular atrophy, but a typical example presents a single clearly marked crescentic notch in the centre of the cutting edge, and the tooth is peg-shaped, short, and narrow. Less frequently the first permanent molars, usually of the mandible, show rudimentary development of the cusps, which remain rounded and crowded together resembling an unfolded bud (mulberry or Moon's molars).

The early cutaneous lesions of congenital syphilis are infective ; in later years the infectivity is very slight, but syphilis has been shown to be transmitted to the third generation, although such cases are very rare.

Syphilis and Pregnancy

Syphilis associated with pregnancy undergoes considerable modifications. When acquired at the time of conception or during the course of pregnancy there is frequently an inhibition of the early stages ; no primary stage is noted, and secondary lesions are either slight or absent. This latency as regards the mother may persist until the menopause, after which the various tertiary syphilides may become manifest. The majority of these patients have a positive Wassermann test, but this may vary during pregnancy. A positive Wassermann reaction given by the umbilical-cord blood is an indication of infection in the mother and not necessarily in the infant.

The child may suffer from severe syphilis even though the condition be latent in the mother. As a rule, the earlier pregnancies result in syphilitic still-births ; later pregnancies produce living but syphilitic children, and ultimately a normal child may result. The infectivity of the mother to the fœtus may vary in an unaccountable manner, and it is not uncommon to see in a large family a healthy child interposed in age between others bearing manifestations of syphilis.

A child suffering from active congenital syphilis does not infect its mother

although a healthy nurse may become infected. This observation, known as *Colles's law*, depends on the fact that the mother is already syphilitic, usually in the latent stage, and cannot be reinfected. Although there are frequently no clinical signs in the mother the Wassermann reaction is positive.

The Wassermann Reaction

During the course of syphilis certain changes take place in the blood as a result of its reaction to the presence of spirochætes. These are indicated qualitatively, and to some extent quantitatively, by the reaction known as the Wassermann test. Positive results are met with in yaws and in leprosy, but in England a positive result to this test almost invariably indicates syphilis; a negative result, however, as will be noted later, does not invariably exclude syphilis.

In the stage of incubation and in the earlier part of the primary stage the reaction is negative, a positive result being rarely found before fourteen days after the appearance of the primary lesion. From this time until the manifestations of the secondary stage appear there is a gradual increase in the percentage of positive results, the reaction being most markedly positive in the florid stage of secondary syphilis.

In the latent and tertiary stages of the disease the Wassermann test is positive in 60 to 70 per cent. of cases.

The Wassermann test in congenital syphilis with active lesions is positive in 90 per cent. of cases; in the stage of latency the occurrence of a positive reaction is less frequent and in adult life tends to disappear. Following the administration of arsenical remedies or penicillin, the Wassermann reaction may become negative and remain so, provided treatment is both early and efficient.

Various flocculation serum reactions, in which the mixing of syphilitic serum with an alcoholic extract of heart muscle produces visible flocculi, are now also employed in diagnosis. The Kahn reaction, which is most generally used in this country, is slightly more sensitive than the Wassermann reaction.

THE TREATMENT OF SYPHILIS

The modern treatment of syphilis by penicillin, arsenical compounds, and bismuth is followed by extremely favourable results, provided that it is commenced in the early stage and maintained regularly. Any delay in the institution of treatment renders cure less likely. The results of treatment commenced in the sero-negative primary stages are overwhelmingly superior to those begun in any later stage; it is therefore of the utmost importance to establish the diagnosis of syphilis before the advent of a positive Wassermann test, and this can only be done with certainty by finding *Spirochæta pallida* in the serum expressed from the primary lesions.

Since the introduction of the original arsphenamine (Salvarsan or "606") by Ehrlich in 1910 and of neoarsphenamine (Neosalvarsan "914") a few years later, syphilis has been treated mainly by compounds of this type. The drug most frequently in use at the present time is neoarsphenamine, an organic arsenical compound containing about 20 per cent. of arsenic. Although the efficiency of this compound is slightly less than that of the

original salvarsan, its lower toxicity and ease of administration have led to its general use.

Neoarsphenamine is manufactured under various names, *e.g.*, novarsenobillon (N.A.B.), novostab, neokharsivan, and neosalvarsan.

Mapharside and neohalarsine, which are derivatives of phenyl-arsine oxide, are also valuable remedies ; on account of their rapid excretion they should be injected twice each week.

Bismuth also is used in the treatment of syphilis in conjunction with the organic arsenicals. Numerous preparations are advocated of which the metallic suspensions or bismuth oxychloride are the most suitable. The repeated injection of bismuth may cause albuminuria or gingivitis ; the latter is usually dependent upon associated pyorrhœa. Any dental sepsis present should receive attention.

Mercury by injection is now little used but is sometimes given orally as liquor hydrargyri perchloridi ($\frac{1}{2}$ to 1 drachm), or pulvis hydrargyri cum creta (1 to 5 gr.) in the later stages.

In cases of primary and secondary syphilis a neoarsphenamine preparation is administered without delay. For men of average weight and otherwise in good health the initial dose is 0·45 gm. This is followed by eight weekly intravenous injections of 0·6 gm. increasing to 0·75 gm. in men over eleven stone in weight. Each week during this treatment a bismuth preparation equivalent to 0·2 gm. of bismuth metal is injected into the muscles of the buttock.

In women the average initial dose of neoarsphenamine is 0·3 gm., and subsequent doses should not exceed 0·6 gm. For men or women of less than average weight, or in slightly impaired health from concurrent disease, the individual dosage is slightly reduced.

Such a series of injections constitutes a course of treatment. After an interval of four weeks a second similar course is administered followed by a similar rest interval.

A Wassermann test is done at the beginning of each course. In all at least four such courses should be given to cases in which the Wassermann reaction is negative after the first course.

A small proportion of cases will fail to become negative after as many as six courses. Before prolonging treatment, attention should be paid to the general health and to signs of syphilitic involvement of the central nervous system.

When intravenous injection is difficult the treatment may be continued by intramuscular injections of sulpharsphenamine compounds, *e.g.*, sulphostab or kharsulphan, 0·3 to 0·45 gm.

When gross intolerance to arsenical compounds is evident, courses of penicillin and bismuth treatment are relied upon.

During pregnancy, injections of penicillin, neoarsphenamine, and bismuth are well tolerated and can be administered up to the eighth month ; the risk of abortion is very slight. With efficient treatment throughout pregnancy there is a minimal risk of congenital disease in the child.

Penicillin has a marked healing effect on syphilitic lesions. Spirochætes disappear within twelve to twenty-four hours, and the chancre or the cutaneous and mucous membrane lesions of the secondary stage heal rapidly. Large amounts of penicillin, however, and numerous regular injections are necessary to produce a permanent effect. Penicillin is now used as a routine

in the treatment of syphilis in the primary and secondary stages, although obviously many years must elapse before its final value can be assessed.

The standard treatment consists of a total dosage of 3,600,000 units given in sixty consecutive intramuscular injections of 60,000 units, each at three-hourly intervals day and night for seven and a half days. Calcium penicillin in an oil-wax medium is also used for ambulant cases of syphilis ; doses of 450,000 units are given intramuscularly once a day for eight days. Toxic reactions from penicillin are rare and trivial. The Herxheimer reaction, however, is more frequent than with other antisyphilitic remedies. A focal reaction of this type such as increased swelling of the chancre or a temporary exacerbation of the secondary rash is often seen : the systemic Herxheimer reaction—fever of moderate degree ensuing after the first or second injection —occurs in about one-half the cases.

After penicillin treatment the positive serological reaction usually becomes negative within three to four months. When penicillin is used alone in cases of early syphilis a relapse occurs in about 10 per cent. within a year. Increasing the dosage has not succeeded in preventing relapses. For this reason penicillin should be followed by treatment with at least one course of neoarsphenamine and bismuth. Following combined treatment with penicillin, arsenicals, and bismuth a Wassermann test is done every third month during the first year after treatment and every sixth month during the next two years. The cerebrospinal fluid should be examined during the first year. When all these tests have been negative the patient may be considered to be cured.

Congenital Syphilis.—Syphilitic conditions arising in infancy respond well to treatment, which follows the same general lines as in adults.

The rapid action of penicillin on syphilitic lesions and its freedom from toxic effects renders it a most valuable remedy for congenital syphilis, especially in the premature infant. Penicillin therapy should be started as soon as the diagnosis is made. The dosage advised is 1,000 units of sodium penicillin per pound weight of the infant, given at four-hourly intervals for eight days. On account of the possibility of a severe Herxheimer reaction in premature and feeble infants a small pilot dose should be given twenty-four hours before the main treatment is started. Penicillin given orally with each feed is also effective ; the most suitable dosage is not yet decided but is probably about 10,000 units per feed, which is maintained for fourteen days.

Penicillin therapy should be followed by further treatment with at least two courses of injections of an arsenical compound and of bismuth. The toleration of infants and children for these remedies is excellent. In infancy the disease is treated with acetylarsan (diethylamine acetarsone) or sulpharsphenamine given by intramuscular injection. Intravenous injection of neoarsphenamine, whilst efficacious, is difficult in children under the age of five years. Acetylarsan is particularly suitable for the premature or feeble infant to whom 0·2 to 0·3 c.c. of the dilute solution designed for infants may be given each week.

In older infants arsenical treatment may be commenced with sulpharsphenamine. For an infant three months old the initial amount is 0·05 gm., increasing each week gradually up to 0·1 gm. in a course of ten weekly injections. A few weeks later a bismuth preparation, *e.g.*, a metallic bismuth suspension or bismuth oxychloride, is injected into the gluteal muscles in weekly amounts equivalent to 0·02 gm. of bismuth metal. for a period of ten weeks.

Older children require larger amounts of these compounds. For a child one year old and of average weight ten weekly injections of sulpharsphenamine are advisable, the amount increasing from 0·05 to 0·15 gm. These are followed by the equivalent of 0·04 gm. of bismuth metal in each of ten weekly injections

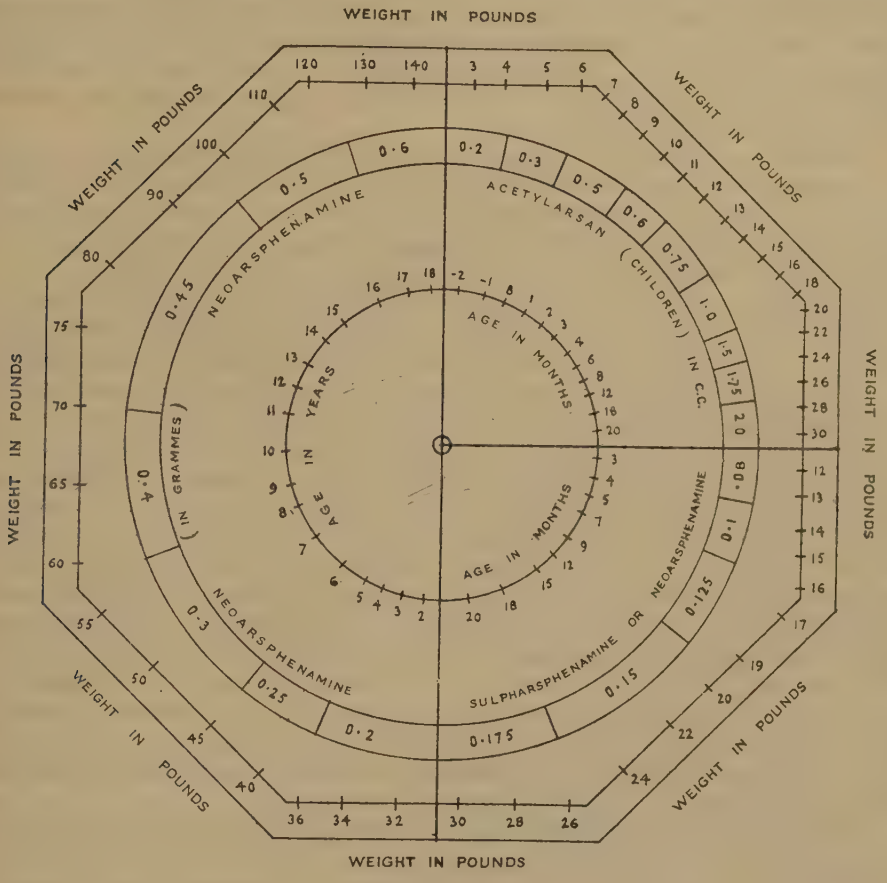


FIG. 6

TREATMENT TARGET FOR CONGENITAL SYPHILIS

How to Use the Target

A straight line joining the target centre to the mark indicating the weight of the child will cross through the block bearing the appropriate maximum weekly dose of the various arsenical compounds.

The inner circle bearing age figures is included as a useful and rapid indicator of the average weight of a child for a given age. A straight line connecting the target centre to the notch indicating the age of the child will pass on through the figure for the average weight for that age.

The dosage indicated in the chart has been calculated chiefly from the weight of the child but at certain ages it has been raised in proportion to the higher basal metabolic rate.

Since children suffering from syphilis are frequently debilitated and under weight, the amounts to be given of these remedies should be considered in terms of weight of the infant rather than of its age. In general, after the age of three months, children of any age may be given 0·005 gm. of sulpharsphenamine or neoarsphenamine for each pound weight as the maximum weekly

amount in a series of injections. The initial amount should be about 0·002 gm. for each pound of the child's weight. Thus for a child weighing 30 lbs. the initial amount should be 0·06 gm. and the maximum weekly amount 0·175 gm. In older children the intravenous injection of neoarsphenamine is usually practicable and is advised. The continuation of each course and the progressive increase in dosage depends upon the improvement in the local and general condition, a progressive gain in weight, and the absence of signs of intolerance to arsenic. The accompanying chart (*vide* Fig. 6) provides a rapid method of ascertaining the appropriate dose of the various arsenical compounds for a child of any weight.

The series of arsenical injections is followed by a series of ten weekly injections of bismuth. At the age of three to six months amounts equivalent to 0·02 gm. increasing to 0·03 gm. are given. As an approximate guide to dosage the equivalent of 0·01 gm. of metallic bismuth for each 5 lbs. of the child's weight may be considered as being the maximum weekly dose.

Potassium iodide is not well tolerated in infancy. Syr. ferri iodidi (5 minims t.d.s.) is preferable ; this may be given during treatment with arsenicals or bismuth and is useful in promoting resolution of visceral syphilitic conditions.

After apparently efficacious treatment the child must be subjected to close periodic clinical and serological observation until the adolescent age. The cerebrospinal fluid should be examined in all cases having a positive blood Wassermann reaction after a year's treatment. Apparent clinical cure with negative blood tests is attained in most of the cases when treatment is begun in infancy. In older children who have been infected for some years before treatment is commenced the blood may remain positive in spite of prolonged treatment over several years ; the state of the child's general health and development is then the best guide to the advisability of further treatment. The well-known hall-marks of congenital syphilis—Hutchinson's teeth, rhagades, and saddle-nose—are permanent and are entirely unaffected by treatment. Nerve deafness is little if any improved and interstitial keratitis may be protracted or may recur, but the final response is reasonably good. The neurological disorders of late childhood, such as tabes dorsalis and general paralysis, are best treated by malaria and penicillin.

Treatment of Tertiary Syphilis.—The general condition of the patient, and in particular the state of the lungs, heart, liver, and other vital organs, must be considered. In these late cases much harm to the general health may be caused by injudiciously intensive treatment with organic arsenical remedies at a time when the complete eradication of syphilis is probably impossible. The main object of treatment at this stage is to keep the patient reasonably well and not to attempt to sterilise the tissues, possibly at heavy cost to the general health.

In general, treatment should be mild in intensity but prolonged. It should commence with potassium iodide, 30 to 60 gr. daily, which has a marked absorptive action on gummatous deposits. Penicillin should be given in one daily injection of 250,000 units of a calcium penicillin oil-wax suspension for seven days. Neoarsphenamine is given later, in small or moderate amounts, at intervals of one or two weeks. Intravenous injections should not be given to patients over sixty years old. Arsenic and bismuth injections are given in separate courses.

A pregnant woman suffering from syphilis in any stage requires intensive treatment if the health of the child is the main consideration.

Gummatous lesions of the skin, mucous membranes, and soft skeletal structures react readily to treatment. In visceral gummata there is a rapid initial effect but final resolution may be slow. The effect of treatment upon the late syphilitic affections of bone is very slow although symptoms may disappear promptly. Elderly patients suffering from tertiary syphilis whose indifferent health is partly due to additional causes are best treated by penicillin, the prolonged use of bismuth injections and iodides.

The treatment of cardio-vascular syphilis and neurosyphilis is dealt with elsewhere (*vide* pp. 434 and 646).

The Toxic Effects of the Organic Arsenical Compounds

The various toxic effects of these arsenical preparations themselves may be divided clinically into an early and a late group.

Early Reactions.—Nausea and vomiting, either during or immediately following an intravenous injection, are commonly met with ; some hours later there may be mild diarrhœa or, rarely, transient jaundice.

Following the first or second intravenous injection there may occur, but rarely, a group of symptoms which has been termed " nitritoid crisis " or " vasomotor crisis." This reaction, which ensues during or immediately after the intravenous injection, consists of the sudden onset of dyspnœa, dilatation of the pupils, cyanotic flushing, and tingling of the hands and feet, which are followed rapidly by varying degrees of transient unconsciousness. Later, œdema of the face, especially the lips and eyelids, may follow.

Transient cutaneous eruptions of general distribution, either erythematous or urticarial in type, may supervene at any time within the first two days after injections. Such reactions are likely to be repeated after further injections.

The most serious of these early reactions is acute encephalopathy, which supervenes within twenty-four to thirty-six hours ; this complication is very uncommon but is usually fatal. Purpura hæmorrhagica is a rare toxic effect, but even if mild is a warning of a dangerous idiosyncrasy to arsenic ; such cases may develop aplastic anæmia. Agranulocytosis may also occur.

Prevention and Treatment.—Intravenous injections of anti-syphilitic remedies should not be administered within two hours of any heavy meal, and all solutions should be freshly prepared and administered slowly. The most efficient treatment for the vasomotor reaction is an immediate subcutaneous injection of 1 c.c. of a 1 in 1,000 solution of adrenaline. The cutaneous eruptions, acute encephalopathy, and blood dyscrasias are treated with BAL.

Late Toxic Reactions.—During active treatment over long periods, minor toxic effects such as general malaise, depression, and loss of weight may occur at any time. Peripheral neuritis giving rise to paræsthesiæ and, later, drop-foot is a rare complication.

Arsenical Dermatitis is usually an acute generalised eruption of the exfoliative type associated with intense irritation ; in mild cases it may not progress beyond the erythematous or papular stages, in which case it is likely to be taken for a simple erythema, or, if papular, for lichen planus.

In the severe type an initial acute general erythema with some infiltration of the skin and mucous membranes is soon followed by the formation of

vesicles and bullæ ; the condition progresses rapidly into a state of acute weeping dermatitis, with crusting and exfoliation. Secondary infection of the raw surfaces is a common sequel, and abscess formation may take place in the axillary, inguinal, or cervical glands. The condition is protracted, and some of these cases are fatal from broncho-pneumonia or œdema of the lungs.

Unlike the earlier toxic reactions, arsenical dermatitis supervenes after some weeks or months of treatment.

Treatment.—Complete rest in bed, application of calamine lotion or olive oil, and intramuscular injections of BAL (2, 3-dimercapto-propanol), 2 c.c. at four-hourly intervals during the first twenty-four hours, 2 c.c. twice daily on second, third, and fourth day, and 2 c.c. once daily on fifth and sixth days. Scrupulous care should be taken in dressing any raw areas to avoid infection.

Jaundice.—Whilst well known as one of the rarer signs of secondary syphilis, jaundice may occur during the first few weeks of arsenical therapy in any stage of the disease. Jaundice occurring several weeks or months after a series of injections is now regarded as being due to infective hepatitis, most probably transmitted by the use of imperfectly sterilised syringes which have been contaminated by the virus from other patients.

The appearance of excess of urobilinogen in the urine during treatment with arsenicals or the detection of a rise in the bilirubin content of the blood serum is an indication for the cessation of arsenical treatment, which may prevent the production of any further damage to the liver.

Treatment.—As for infective hepatitis (*vide* p. 343) together with injections of BAL for six days.

V. E. Lloyd.

TROPICAL DISEASES [1]

INTRODUCTION

ALL those diseases which are commonly met with in temperate countries are encountered also in tropical and subtropical climates. The quest for tropical diseases should not tempt the practitioner to overlook conditions which he would readily recognise at home. Except in epidemics and in particular areas it is unlikely that more than a small percentage of the patients who seek medical advice will do so on account of purely tropical disease. Moreover, residence in hot climates has effects on the physiological processes of the body for which due allowance must be made, and a dual pathology is far more often present than in temperate climates.

No branch of medicine offers greater scope for preventive measures. The great majority of the incapacitating and killing diseases of the tropics are conveyed by arthropod vectors. In some the causative organism has an essential cycle of development in the arthropod, in others the arthropod passes on the organism mechanically. In still other diseases water is the medium of infection. In all these conditions treatment of the individual who has become infected is a poor substitute for the attention to hygiene and sanitation that could have prevented such infection. Some knowledge of the life-cycles and habits of the various hosts and vectors and an acquaintance with the sanitary measures appropriate for their destruction or control are therefore essentials of tropical practice.

MALARIA

Malaria is the most important of all the tropical diseases, being responsible for several million deaths every year and for an incalculable amount of invalidism. Although far more common in tropical and subtropical countries, it occurs also in temperate zones.

Ætiology.—The disease is caused by protozoal parasites of the genus *Plasmodium* which are conveyed from man to man by female anopheline mosquitoes. Only three species of plasmodia are of importance, *P. falciparum* causing malignant tertian (subtertian), *P. vivax* causing benign tertian, and *P. malariæ* causing quartan malaria. These plasmodia have essential phases of development and multiplication in the mosquito and in man. The *sexual* phase occurs in the mosquito and occupies about ten days. It is initiated by the union of a pair of sexually differentiated parasites (gametocytes) taken up from the blood of man when the mosquito feeds. The final products of this union (sporozoites), many hundreds of which are produced, are injected into man by the mosquito when it feeds again. These sporozoites initiate the *asexual* cycles in man. It used to be thought that each sporozoite invaded a red corpuscle but it has long been known that in birds and monkeys

[1] Helminthic infections and the dietary deficiencies are dealt with in other sections.

the sporozoites pass through one or more exoerythrocytic cycles of development in various organs before they enter the red cells. Assumptions based on sub-inoculation and therapeutic experiments suggested that a similar development occurred also in man. Experimental biopsy in man has recently shown these assumptions to be correct. It is thought that, whereas in falciparum infections the exoerythrocytic cycles are completed in about a week, in vivax infections parasites may continue to emerge from the exoerythrocytic into the erythrocytic stage over a period of months or even years.[1] Sooner or later, however, parasites are produced which invade the

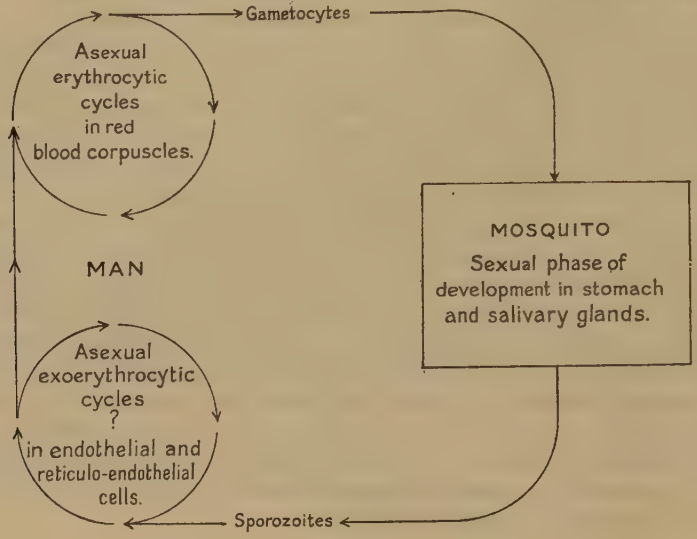


FIG. 7

The Life-cycle of the Malaria Parasite.

red corpuscles in which further multiplication occurs. This erythrocytic cycle differs somewhat in the various species, causing fever at regular intervals according to the duration of the cycle of the species concerned—about thirty-six hours for *P. falciparum*, forty-eight hours for *P. vivax*, and seventy-two hours for *P. malariæ*. Each cycle culminates in the rupture of infected red cells from each of which are liberated parasites which invade yet other red cells. Some of these parasites become sexually differentiated and develop into male and female gametocytes. These alone can initiate the sexual cycle when taken up by a mosquito.

Control of Malaria.—For the occurrence and continued existence of malaria there must therefore be :—

1. Vectors of the infection, female anopheline mosquitoes.
2. Infected persons (having gametocytes in their blood) from whom the mosquito may derive its infection.
3. Susceptible persons to whom the infection may be transmitted.

[1] This explains not only the interval that elapses between infection and the appearance of parasites in the blood but also the rationale of relapses. Moreover, it becomes clear why vivax malaria cannot be *radically* cured by drugs which, however effective they may be against erythrocytic forms, are not lethal to the exoerythrocytic stage.

4. Opportunities for the mosquitoes to bite both infected and susceptible persons.

If any one of these essentials could be completely eliminated malaria would cease to exist. As this is impossible in practice, control of the disease involves the prosecution of measures directed against all four, namely :—

Anti-mosquito measures which must be adapted to the habits of the particular species responsible and directed against—

(*a*) the aquatic larval forms in their breeding places by the application of larvicidal oils or dusts to the surface of the water, by clearing streams and by canalising, draining or filling in marshes and swamps ;

(*b*) adult mosquitoes by the use of insecticidal sprays in their resting places. The destruction of mosquitoes in native houses (the main source of infected mosquitoes) has proved a most effective measure of control, and D.D.T.,[1] because of its prolonged residual action, has now made this an economic proposition.

Prevention of mosquito bites by the use of protective clothing and nets during the hours of darkness. Ideally, all living quarters should be screened with mosquito-proof gauze. Repellent lotions such as indalone or dimethyl phthallate applied to exposed parts of the body or to the clothing give some protection, but their application is wearisome and their effect short-lived.

Thorough treatment of all cases of malaria to prevent their becoming gametocyte carriers and thus forming a reservoir of infection to mosquitoes.

Suppressive Therapy.—In hyperendemic areas, and especially when sickness must be avoided at all costs (as in military operations when other methods of control may be impracticable), malaria can be suppressed by drugs. Quinine, mepacrine,[2] several of the sulphonamides, and the 4-amino quinoline [3] compounds will suppress infections and may *eventually* produce radical cure by destruction of the erythrocytic forms alone. Pamaquin [4] destroys the exoerythrocytic forms of *P. falciparum* and inhibits those of *P. vivax*, but is relatively ineffective against the erythrocytic forms and is, moreover, too toxic a drug to be used indiscriminately. Paludrine [5] not only combines the effects of all these drugs but is harmless even in many times the necessary dosage. Thus both pamaquin and paludrine are causal prophylactics [6]—partial against vivax and complete against falciparum infections—and paludrine is the drug of choice. Optimum dosage is not yet universally agreed but 0·1 gm. (one tablet) twice a week gives complete protection against clinical malaria so long as that dosage is continued and completely prevents the development of falciparum infections. Moreover, the blood of persons taking this dosage sterilises both vivax and falciparum infections in mosquitoes feeding on them. Mepacrine in a dosage of 0·1 gm. (one tablet) daily will also suppress clinical malaria and, although it has several minor disadvantages, should be used if paludrine is not available.

Suppressive therapy by mepacrine must be begun at least ten days before exposure to infection. Paludrine, on the other hand, gives almost immediate

[1] D.D.T. = para para dichloro-diphenyl-trichlorethane, a powder, insoluble in water, which, even in very high dilution, is extremely toxic to practically all arthropods. A surface of 500 to 1,000 sq. ft. sprayed with a quart of a 5 per cent. solution in kerosine remains lethal for many weeks to insects alighting on it.

[2] Mepacrine, an acridine derivative. Synonyms : atebrin, quinacrine, atabrine (U.S.A.).

[3] *E.g.*, sontochin (chloroquin) and resorchin (aralen).

[4] Pamaquin, an 8-amino quinoline. Synonyms : plasmoquine, plasmochin (U.S.A.).

[5] Paludrine, a biguanide recently synthesised in England.

[6] A causal prophylactic is a drug which prevents plasmodia invading the red blood corpuscles.

protection. After leaving a malarious area suppressive therapy should be continued for six weeks, no matter which drug has been used.

No known drug in safe dosage will destroy sporozoites.

Pathology.—In the acute stage of malaria, especially in subtertian, blockage of the capillaries of various organs by infected red cells causes local congestion, œdema and stasis. The rupture of numbers of infected red cells liberates, in addition to a new generation of parasites, hæmoglobin from the cells and a dark pigment from the parasite itself. This pigment possesses toxic and hæmolytic properties, and there follows a progressive anæmia, toxæmia, hæmoglobinæmia, and pigmentation of the cells and organs of the reticulo-endothelial system. The liver and spleen enlarge as they attempt to deal with the products of hæmolysis, while the efforts at blood regeneration are reflected in hyperplasia of the hæmopoietic tissues.

Symptoms.—After an incubation period of one to three weeks or more, the first bout of fever occurs. Onset is sudden, usually with a rigor. There are three well-marked stages.

1. *The Cold Stage.*—The patient shivers, the teeth chatter, and the skin is blue and "goosey," and he piles on all the bed-clothes he can find. There is headache and often vomiting. The sensation of cold is purely subjective as the temperature is already rising. This stage lasts for one or two hours.

2. *The Hot Stage.*—The patient begins to feel hot and the headache grows worse. The bed-clothes are thrown off, the skin becomes flushed and dry and the pulse full and rapid. The temperature rises to 104°, 105°, or even higher. This stage lasts from three to four hours.

3. *The Sweating Stage.*—Gradually the skin becomes moist, the patient breaks into a profuse sweat, saturating the bed-clothes, and the temperature begins to fall. After two to four hours the sweating ceases, the temperature falls to normal, and the patient may feel so much better that it may be difficult to prevent his going to work.

In benign tertian malaria, attacks recur on alternate days until cut short by treatment, while in quartan malaria there are two clear days between attacks. When mixed or multiple infections are present this regular sequence is broken. Sometimes the rigor may be absent and one or other of the stages is shortened or lengthened.

In malignant tertian infections the onset is often insidious, rigors may be absent and the stages are less well defined. Pyrexial periods may be prolonged and apyrexial periods shortened so that fever is often quotidian or remittent. Such is the textbook picture. In practice there is scarcely a symptom that malaria may not produce and, equally, almost every expected symptom may be absent. This applies especially in first attacks and in those who have acquired some degree of immunity or are taking suppressive drugs in irregular or inadequate dosage.

Malignant Malaria.—Any case of subtertian malaria is liable suddenly to develop pernicious symptoms which may kill the patient with hardly any warning. For this reason every case should be regarded and treated as an emergency. These pernicious cases occur most commonly in hyperendemic areas, at the most malarious season of the year, and in initial attacks. They are nearly always due to infection with *P. falciparum.* They fall roughly into two main types—cerebral and algid.

The *cerebral type* may be characterised by hyperpyrexia with wild delirium terminating in fatal coma. Sometimes coma may supervene without any

warning. Convulsions may occur, and pareses and permanent mental changes may result.

The *algid type* causes shock, collapse, and a tendency to fatal syncope. Gastric, dysenteric, pneumonic and hæmorrhagic forms also occur.

These pernicious types are caused by obstruction of the capillaries of the various organs by parasitised red cells.

Relapses.—Benign tertian and quartan malaria are very liable to relapse for many months or even years after the original attack. These relapses may be explained by the delayed emergence of exoerythrocytic forms which cannot be destroyed as such by even the most thorough treatment.

In falciparum malaria, in which this delay does not occur, relapses must be due to survival and multiplication of erythrocytic forms alone. Thus relapses occur sooner and during a much more limited period and are rare after thorough treatment, since radical cure should be attainable by any one of the several drugs which are effective against the erythrocytic forms.

Relapses are apt to be precipitated by illness, shock, chill, surgical operations, and too early cessation of suppressive therapy. If the original attack was suppressed by drugs, a relapse, perhaps long afterwards, may be the first clinical manifestation of malaria.

Chronic Malaria.—In the absence of adequate treatment, especially following repeated reinfection, malaria tends to become chronic. The spleen enlarges, often to many times its normal size, but eventually becomes small, fibrosed, hard, and of a slaty colour, the typical "ague cake" spleen. The liver undergoes somewhat similar changes. Cachexia develops with a skin jaundiced by chronic hæmolytic anæmia. A leucopenia with a relative monocytosis is usually present. General debility renders the patient an easy prey to intercurrent disease.

Immunity.—There is probably no natural immunity to malaria. A considerable immunity can be acquired over a period of years but only at a great risk to life and at the price of prolonged illness.

Diagnosis.—Owing to the protean nature of the symptoms, malaria may resemble almost any febrile disease, and the short fevers, such as sandfly fever and dengue, are, perhaps, those most likely to be confused with it.

Although malaria is a disease in which an early and accurate diagnosis is normally to be expected, yet in some cases, especially subtertian or when suppressive drugs have been taken, parasites may be absent from the peripheral blood. In such cases treatment must be started at once without waiting for proof of the diagnosis.

If it has not been possible to make the diagnosis by blood examination, the response to anti-malarial drugs may supply it. When a fever continues in the absence of parasites and despite the administration and absorption of these drugs, it is unlikely to be malaria. On the other hand, there are many short fevers (*e.g.*, sandfly fever) which will appear to respond, since the temperature drops in any case after two or three days whether or not anti-malarial drugs are given. Moreover other acute fevers may occur in a patient with latent malaria, so that the discovery of parasites may not supply the whole diagnosis.

Treatment.—Until a drug is discovered which is lethal to both the erythrocytic and exoerythrocytic stages of all the human plasmodia and which is not toxic to man, the treatment of malaria will remain uncertain. The synthesis of paludrine has gone far towards this ideal.

Most of the drugs in use relieve symptoms and control fever by destruction of the erythrocytic forms alone. They cannot effect radical cure so long as parasites remain in the exoerythrocytic stage. In falciparum infections, therefore, radical cure is possible since, by the time treatment is given, all parasites are likely to be erythrocytic. Moreover, in paludrine and pamaquin, we have the means of destroying the exoerythrocytic forms of *P. falciparum*. But, in other infections, although rapid clinical cure is obtainable, relapse occurs almost inevitably sooner or later when treatment is discontinued. In these cases (since even paludrine and pamaquin have only an inhibitory effect on the exoerythrocytic forms) therapeutic treatment must be followed by suppressive treatment for a long period to destroy parasites as they emerge into the erythrocytic stage and until the infection can be expected to have died out.

Mepacrine is more effective than quinine, is less toxic and less liable to precipitate blackwater fever. It has the æsthetic disadvantage of causing a yellow discoloration of the skin, but this is a useful proof of absorption. Quinine has the single advantage of rather more rapid action. While paludrine and pamaquin both destroy exoerythrocytic forms of *P. falciparum* and inhibit the development of those of *P. vivax*, paludrine is lethal also to the erythrocytic forms. Pamaquin has little effect on these. Moreover, paludrine is a safe drug ; pamaquin is not. Paludrine is therefore the drug of choice in the treatment as in the chemoprophylaxis of malaria. In its absence mepacrine should be used in preference to quinine.

Treatment of Acute Malaria.—A severely ill patient in whom malaria is a possibility must be treated at once. To wait until parasites have been found will result sooner or later in a fatality. When the clinical urgency of the case demands immediate measures, it also usually demands the more rapid effect obtained by intravenous medication (*vide* p. 139).

Normally, however, treatment is by mouth. An initial dose of calomel, followed by salts, should be given to open the bowels, and pulv. A.P.C. (Tab. Acid Acetylsalicyl. Co. B.P.C.) to relieve headache and encourage sweating. One of the following courses should be started at once, as soon as a blood smear has been taken :—

Paludrine : 0·1 gm. t.d.s. for ten days. Thereafter, in vivax and quartan infections, 0·1 gm. may be given twice a week for a year to prevent relapse.

Mepacrine : First day, 0·3 gm. t.d.s. ; second and third days, 0·2 gm. t.d.s. ; fourth, fifth, and sixth days, 0·1 gm. t.d.s.

In vivax and quartan infections relapses may be prevented by giving 0·1 gm. daily for six to twelve months. The initial high dosage is necessary in order to produce rapidly an adequate concentration of the drug in the blood.

Quinine : 10 gr. t.d.s. until the temperature has been normal for forty-eight hours. Thereafter 10 gr. b.d. for a week, a week's rest from treatment, and 10 gr. b.d. for a further week. Quinine should always be given in solution. When given by mouth it is immaterial which salt is used, but the relatively insoluble sulphate requires the addition of acid to effect solution. Quinine in therapeutic doses nearly always causes nausea and tinnitus and, not infrequently, vomiting, palpitations, and deafness. In rare cases of idiosyncrasy, amblyopia, hæmoglobinuria, and urticaria may occur. There is much to be said for avoiding oral quinine altogether and for reserving the drug for intravenous use in emergency.

Some authorities like to give pamaquin in a dosage of 0·01 gm. t.d.s. for four or five days as an adjuvant to any of these drugs, since it has been shown to reduce the liability to relapses or, at least, to postpone their occurrence. It should not be given concurrently with mepacrine, which seems to enhance its toxicity, and there is little reason for prescribing it if paludrine is used, but it is a useful addition to quinine or mepacrine, especially in the absence of subsequent suppressive therapy. It should be remembered that it has no immediate clinical effect.

If the temperature is not normal by the third day of any course of treatment, and tests show that the drug in use is being absorbed, the diagnosis should be reviewed.

The patient should be kept in bed until the temperature has settled and should be nursed under a mosquito net in endemic areas. Abundant fluids, glucose, and alkalis by the mouth are a wise addition to treatment. An iron and arsenic tonic should follow if there is demonstrable anæmia.

Intravenous Therapy.—In all cases presenting pernicious symptoms, and particularly in cerebral malaria, intravenous quinine should be administered at once. The risk of sudden and fatal collapse due to rapid destruction of large numbers of parasites and the liberation of toxins into the circulation has been somewhat exaggerated and is not to be compared with the risk to life of withholding treatment in a severely ill patient. The dose is 10 gr. It should be diluted in at least 20 c.c. of sterile normal saline, preferably more, and at least ten minutes should be taken over its introduction. Repetition is seldom necessary, further treatment being given by mouth or intramuscularly. It is not advisable to administer mepacrine intravenously. Intravenous paludrine has been used but has not yet replaced quinine.

Intramuscular Therapy.—Intramuscular quinine has many disadvantages and few advantages over the intravenous route, but when veins are collapsed, or the operator is inexperienced, intramuscular therapy may be preferable. The dose is 8 to 10 gr. of the bihydrochloride dissolved in 1 to 4 c.c. of sterile saline or distilled water. Great care must be taken to give the injection deep into the gluteal muscles, well clear of the sciatic nerve, and because the intramuscular injection of quinine always causes some degree of local necrosis, the strictest aseptic precautions are essential. The dose rarely needs to be repeated more than twice.

Mepacrine methane-sulphonate [1] may be given intramuscularly as an alternative and may act more rapidly than mepacrine by the mouth, but probably not so rapidly as intramuscular quinine. The dose is 0·3 gm. in 2 to 4 c.c. of sterile doubly distilled water. Two or three doses may be given in the twenty-four hours, if necessary.

Treatment of Chronic Malaria.—If every attack of malaria is treated as it occurs and suppressive therapy is used to prevent relapses, there is no need for the prolonged, intensive courses that used to be prescribed. Indeed, in those for whom adequate treatment is available, malaria should never become chronic.

Persons who have had malaria should receive a course of treatment before arrival in a cold climate and should continue their suppressive therapy for six weeks thereafter.

[1] Synonyms: quinacrine soluble, atebrin musonate.

BLACKWATER FEVER

Blackwater fever is characterised by an acute hæmolysis of the red blood cells resulting in a hæmoglobinæmia, and when the renal threshold has been passed, hæmoglobinuria or "black-water."

The geographical distribution is superimposed on that of malaria, but is far more limited, occurring only in certain of those areas where severe malaria is prevalent. The reasons for the localised distribution and for the occurrence of hæmolysis are not known. It is now generally agreed that malaria, especially severe and repeated attacks of subtertian, is the essential ætiological factor, and that drugs that are specific in the treatment of malaria, especially quinine, may predispose to the condition. It is rarely seen in persons who have lived in endemic areas for less than a year, but may occur within a year after leaving them. Quinine alone may cause hæmoglobinuria but not black-water fever, and the disease has been reported in persons who have never taken quinine, but it has never been known to occur in persons who have not been exposed to subtertian malaria. It may be stated with certainty that the disease nearly always follows heavy and repeated infections with subtertian malaria that have been irregularly or insufficiently treated, although it may not be possible to find malarial parasites in the blood once the disease has supervened.

The main symptoms are those of a malarial attack with severe and sudden hæmolysis which may involve 50 per cent. of the red cells. This extensive hæmolysis results in the plugging of the renal tubules by insoluble acid hæmatin, but this is probably not the essential feature in the very complex pathology, since the main renal changes are those of tubular degeneration. Loss of kidney function is probably due to vascular changes resulting in renal anoxia, anuria, and uræmia (*cf.* crush syndrome, *vide* p. 516). The urine, which is scanty, with abundant albumin and casts, varies in colour from red to brown or black. There is usually vomiting and epigastric pain. The liver and spleen enlarge as the reticulo-endothelial system attempts to deal with the products of hæmolysis. By the fourth day the hæmoglobinuria lessens and the temperature falls, but relapses may occur. Hyperpyrexia, delirium, persistent vomiting, hiccup, profuse diarrhœa, and oliguria are bad prognostic signs. Mortality varies from 10 to 50 per cent.

There is no specific treatment. Careful nursing is of supreme importance. The patient must be kept at absolute rest in bed and must not be moved. To guard against anuria and acidosis, large amounts of fluid should be administered by mouth and, if necessary, parenterally. Renal damage is minimised if the urine can be kept plentiful and alkaline, but recent work indicates that the quantity of urine is more important than the reaction, and that alkali therapy should be used cautiously. Hot fomentations may be applied over the kidneys, and caffeine citrate in a dose of 2 gr. b.d. may be used as a diuretic. If symptoms are severe, intravenous infusions of glucose (5 per cent.) or sodium bicarbonate (150 gr. to the pint) are indicated. Infusions of plasma have been recommended, but blood transfusions should be reserved for cases with severe anæmia. Quinine should be withheld, but, if parasites are found to be present, full doses of paludrine or mepacrine should be given. Thorough anti-malarial treatment should invariably be given during convalescence. The patient should leave the endemic area

as soon as he is fit to travel and should not return. One attack predisposes to others, which tend to increase in severity.

LEISHMANIASIS

Leishmaniasis occurs in two forms, one generalised, the other localised. Both are caused by various morphologically indistinguishable species of *Leishmania*, minute protozoa closely related to the Trypanosomes, which are transmitted by sandflies (*Phlebotomus*).

Generalised Leishmaniasis. (Kala-azar.)

Kala-azar is a chronic febrile disease caused by *Leishmania donovani*. It occurs most commonly in India and China, but also in Africa, South-eastern Europe, and South America. On the Mediterranean littoral, infants and young children are especially affected, and the disease is called Ponos or Infantile Kala-azar, while the causative organism is referred to as *L. infantum*. In this area, dogs are frequently infected and may act as reservoirs of infection.

Signs and Symptoms.—The onset may be sudden or insidious. There is chronic fever which typically shows two peaks in the twenty-four hours with long periodical apyrexial intervals. The spleen is enormously enlarged and the liver to a lesser degree, causing a great increase in the size of the abdomen in striking contrast to the wasting of the chest and limbs. A marked leucopenia accompanies a progressive anæmia with normal colour index, and hæmorrhages may occur. In Europeans the skin develops an earthy tint and may show areas of dusky pigmentation. The patient generally feels surprisingly well and has a clean tongue and a good appetite, although his temperature may be appreciably raised. In a few cases, despite adequate treatment, depigmented patches occur on the skin and are later replaced by nodules (post kala-azar dermal leishmanoid) which may closely resemble leprosy. After many months or years the untreated patient dies of exhaustion or intercurrent disease to which the leucopenia renders him particularly liable.

Laboratory diagnosis rests on the discovery of leishmania in smears or cultures of blood, sternal marrow, or lymph gland fluid. Splenic puncture is seldom necessary and is not entirely free from danger. Neither the aldehyde test (jellification of the serum by formalin) nor the much more specific complement fixation test is any substitute for the demonstration of leishmania.

Pathology.—The essential fact in the pathology of Kala-azar is the parasitisation and proliferation of the cells of the reticulo-endothelial system.

Treatment.—Antimony is a specific remedy. Tartar emetic (sodium antimony tartrate) in doses not exceeding 2 gr. may be given intravenously in 2 per cent. solution on alternate days for six to eight weeks, but one of the numerous proprietary pentavalent preparations of antimony is now generally used (Pentostam, Neostibosan, solustibosan, urea stibamine, etc.). Stilbamidine (M. & B. 744) has recently been used but has been not infrequently followed by late neuropathies. Pentamidine (M. & B. 800) may be used in antimony resistant cases.

Treatment must be continued until smears and cultures are consistently negative, fever is absent, the spleen is normal in size, the blood picture is normal, and the patient is putting on weight.

Localised Leishmaniasis

1. **Cutaneous Leishmaniasis** (Oriental Sore) occurs in Asia, Africa, South-eastern Europe, South America, and Australia, but is most common in limited areas of India, Iraq, Syria, Palestine, Iran, Arabia, and North Africa, where it has many local synonyms. It is noteworthy that oriental sore and Kala-azar rarely occur in the same geographical area. It is a localised, specific, ulcerating granuloma of the skin of exposed parts of the body and is caused by *L. tropica*. The sore commences as a minute, itching papule, single or multiple. Later it becomes indurated and covered by a scaly crust which is frequently scratched off, uncovering a shallow, indolent ulcer an inch or more in diameter. After three to twelve months slow healing occurs, leaving a depressed scar. A considerable degree of immunity results. *L. tropica* can be found in serum withdrawn in a capillary pipette from beneath the edge of the sore. A course of one of the pentavalent antimony compounds is the best treatment when the sores are multiple. Locally, when secondary infection has been dealt with, cignolin or 2 per cent. antimony ointment may be applied, or emetine, mepacrine (5 per cent.), or berberine may be injected into the edge of the sore. X-rays, ionisation, or carbon dioxide snow may be used.

2. **Nasopharyngeal Leishmaniasis** (Espundia) occurs only in limited areas of South America and is due to infection with *L. braziliensis*. It causes infiltrating sores of the mucous membrane of the mouth and nose, which, though they may heal temporarily, eventually fungate and cause great local destruction. Death from exhaustion or intercurrent disease follows months or years of great suffering, but the condition is amenable to treatment by antimony.

TRYPANOSOMIASIS

African trypanosomiasis (the final stage of which is often called Sleeping Sickness) is confined to tropical Africa, in certain districts of which it is widespread and very fatal, depopulating large areas and causing great desolation.

It is caused by trypanosomes—small flagellate protozoa which infect the blood and are transmitted from man to man by the bite of tsetse flies. Many wild animals and cattle are infected with similar but probably not identical species of trypanosomes.

Two main types of the disease occur and are caused by trypanosomes of different but morphologically indistinguishable species transmitted by different species of tsetse flies.

The trypanosomiasis of the Belgian Congo, the Cameroons, and the Gold Coast is caused by *Trypanosoma gambiense* and is transmitted by *Glossina palpalis* and *Glossina tachinoides*. The disease runs a relatively mild course. The trypanosomiasis of Rhodesia and Mozambique is caused by *T. rhodesiense* and is transmitted by *G. morsitans*. In Tanganyika both forms occur.

Symptoms.—About six weeks after being bitten by an infected tsetse fly the patient starts to have an irregular intermittent fever with various erythematous eruptions, localised œdema, and hyperæsthesia. Later there is a general enlargement of the lymphatic glands, especially in the neck, and of the liver and spleen ; the respiration and pulse-rate are quickened and there is thoracic pain. These symptoms may continue for months or even years, during which trypanosomes can be demonstrated in blood smears. Recovery may take place, but more often the cerebrospinal system is invaded and trypanosomes are present in the brain and cerebrospinal fluid. Although various psychical and even maniacal symptoms may occur at first, the patient gradually becomes increasingly lethargic and somnolent, finally lapsing into coma and dying from exhaustion or intercurrent disease.

Diagnosis rests on the demonstration of trypanosomes in the blood, lymph glands, or cerebrospinal fluid.

Treatment.—Suramin [1] (antrypol), a complex preparation of urea, is the most effective drug in the early stages. Three 1 gm. doses are given intravenously on alternate days and seven more similar doses at weekly intervals. Pentamidine has recently been successfully used. In the later stages Tryparsamide appears to be the drug of choice. A combination of these drugs may be used.

Control and prevention of trypanosomiasis is a huge problem. It involves the study of the habits and breeding places of the various species of tsetse flies with a view to their destruction, and of the role of animals as hosts. Personal prophylaxis is mainly a matter of avoiding the bites of the flies. There is some evidence that suramin may prevent infection.

American Trypanosomiasis, or Chagas' disease, is restricted to limited areas of South America. It is caused by *Trypanosoma cruzi*, which is transmitted by the flying bug *Triatoma*. Armadillos form a reservoir of infection. It causes acute conjunctivitis, facial œdema and adenitis, fever and enlargement of the thyroid gland, liver and spleen. Chronic nervous, myxœdematous and cardiac types are described.

No effective treatment is known.

DYSENTERY

Dysentery means the passage of blood and mucus from the bowel with accompanying colic or tenesmus. The word is, however, generally reserved for two specific diseases, namely, bacillary dysentery usually due to Shiga's, Flexner's, or Sonne's bacillus, and amœbic dysentery due to the protozoon *Entamœba histolytica*. (Dysentery due to Sonne's bacillus is described on page 200.)

Bacillary and amœbic dysentery are by no means purely tropical diseases, but tend to occur more commonly in the tropics because it is there that is found the general disregard of sanitation and hygiene that is necessary for their spread. In temperate climates dysentery is practically limited to institutional outbreaks.

The flagellate protozoon *Giardia* (*lamblia*) *intestinalis* is a fairly common parasite of the small intestine in the tropics. It is often associated with and may be the cause of diarrhœa and abdominal discomfort. The stools

[1] British equivalent of Germanin (Bayer 205) and Moranyl (Fourneau 309).

are typically bulky and of a khaki colour with a peculiar fishy smell. The flagellate or its cysts are easily recognised microscopically. A course of one tablet of mepacrine t.d.s. for five days rarely fails to cure the condition.

Control of Dysentery.—The mode of spread and, therefore, the control of dysentery are the same whether it is bacillary or amœbic. The causative organism is generally transferred from fæces to food by the house fly, though contamination of food and water by dust and by " carriers " may also be important. The disease will therefore occur where there is no efficient system for the disposal of fæces or for their protection from flies pending disposal, where flies and dust are particularly troublesome and food is not adequately protected from them, and where drinking water is not sterilised or obtained from a reliable source.

Control involves the fly-proofing of latrines, the prevention of promiscuous defæcation and the disposal of fæces (in the absence of a water-carriage system) by incineration, burial, or sterilisation. Flies should be dealt with by abolition of breeding places, the incineration of manure and kitchen refuse, and by the use of traps, insecticides, and fly-papers. Food must be protected by thorough fly-proofing of all larders, kitchens, and dining-rooms, and by the use of gauze covers. Food and vegetables that are eaten uncooked should be peeled after thorough washing in strongly chlorinated water. Drinking water, unless its source is above suspicion, must be boiled or otherwise sterilised. Cooks and waiters should be periodically examined to ensure that they are not " carriers," and their personal hygiene should be supervised. Because of the difficulty of applying these measures under active service conditions, dysentery has always been the scourge of armies in times of war and has often been responsible for more casualties than have been inflicted by the enemy.

The spread of the disease by direct contagion is limited to communities where the most elementary sanitary principles are disregarded.

Active immunisation against bacillary dysentery by vaccines has not proved successful.

BACILLARY DYSENTERY

Bacillary dysentery is an acute epidemic disease caused by the invasion of the mucosa of the intestine by *B. dysenteriæ* Shiga or by one of the several strains of *B. dysenteriæ* Flexner. Shiga infections are usually far more severe than Flexner on account of the greater degree of toxæmia caused by the former organism. Sonne dysentery is described on page 200.

Pathology.—Generally speaking, dysentery bacilli do not occur outside the intestinal canal, and do not invade the submucosa. The typical lesions occur in the distal part of the large intestine, but may extend to include the lower third of the ileum, and are due to the action of the toxins produced by the bacilli. In acute dysentery there is at first a general hyperæmia of the mucous membrane and hypersecretion of mucus. Later there are submucous hæmorrhages and diffuse superficial coagulation necrosis with shallow " snail track " ulceration of the transverse folds of the mucosa, forming islands of granulation tissue, serpiginous in outline, surrounded by hyperæmic mucous membrane. In severe cases the necrosis may proceed to actual gangrene so that the mucous membrane is completely destroyed and the gut is contracted into a rigid tube containing green or black sloughs.

Other organs show the signs of acute toxæmia. A fibrotic, stenosed, large intestine may follow. The liability to stenosis will be appreciated if it is remembered that in bacillary dysentery the ulceration spreads round the gut rather than along it.

Signs and Symptoms.—Mild, catarrhal, ordinary ulcerative, fulminating, choleraic, and relapsing types have been described.

After a short incubation period of something less than a week, sudden abdominal pain and an urgent call to stool usher in the disease. Thereafter colic increases, the temperature rises and the frequent motions become less fæcal and contain an increasing proportion of mucus and bright red blood resembling red-currant jelly. Tenesmus, inflammation of the anus and even prolapse of the bowel ensue as the motions increase up to thirty, forty, or even more in twenty-four hours, and the colon can be felt if the abdomen is not too tender to permit palpation.

In fulminating cases the stools may resemble "meat washings," and may even become serous, while in the most severe forms (usually Shiga infections) toxæmia may prove fatal before the number and constitution of the stools has caused alarm. High fever, the passage of offensive sloughs, delirium, and hiccup are grave signs.

A chronic form of the disease may supervene after recovery from the acute attack or may occur occasionally without an acute stage, and is then marked by several daily stools containing blood and mucus, wasting, dyspepsia, and neurasthenia. The descending colon is often thickened and palpable.

Synovitis and arthritis with sterile effusion, especially of the knees and ankles, may occur during the acute stage of the disease, or more usually during convalescence. Conjunctivitis, iritis, parotitis, and peripheral neuritis may also occur as complications and, as they are the result of toxæmia, are more common in Shiga infections.

Diagnosis.—Amœbic dysentery (*vide* p. 146), colitis, malignant disease, diverticulitis, polyposis, and especially malarial dysentery, must be borne in mind and excluded. In acute bacillary dysentery the stools consist almost entirely of bright red blood and viscid mucus and are practically odourless. Microscopically the mucus contains numerous polymorphonuclear leucocytes and red blood cells, a number of large macrophage epithelial cells (which are liable to be mistaken for *Entamœba histolytica*), and scanty non-motile bacilli. There is very little fæcal material.

Although proof of the exact diagnosis must await culture of the causative organism, a tentative diagnosis can usually be made from the cellular characteristics of the exudate and so enable appropriate treatment to be commenced without delay.

Treatment.—Certain measures must be adopted from the outset in all cases of clinical dysentery without waiting for a definite diagnosis. These include strict confinement to bed, starvation diet, and replacement of fluid lost from the bowel.

An initial dose of castor oil followed by saline purgatives for several days was until recently the accepted treatment. Drugs of the sulphonamide group have now generally replaced it and have substantially reduced both the severity of the disease and its tendency to become chronic. Chlorodyne in doses of 20 minims t.d.s. is useful for the relief of pain. Opium and morphia may be given in severe cases.

The poorly absorbed sulphonamides (sulphaguanidine, sulphasuccidine) constitute the treatment of choice. An initial dose of 6 gm. should be followed by maintenance doses of 3 gm. four-hourly until the stools are reduced to about four a day and blood and mucus are absent. Thereafter 3 gm. should be given eight-hourly for a further three days to prevent relapse.

The well-absorbed sulphonamides (sulphathiazole, sulphadiazine) may be used, provided there is no marked dehydration. An initial dose of 2 gm. is followed by 1 gm. three- or four-hourly for the next few days.

Whichever drug is used, precautions must be taken to avoid the toxic effects of sulphonamides (*vide* p. 8).

Diet must be increased very gradually, and not until there is definite clinical improvement, otherwise relapse is likely to result and the disease may become chronic. For the first two or three days, only water, barley water, imperial drink, and tea should be allowed in small quantities at frequent intervals. Thereafter arrowroot, Benger's food, chicken tea, beef tea, and jellies should be added cautiously so that egg flips and milk puddings are being taken by the eighth day and a fish diet by the tenth. Alcohol must be strictly forbidden during the disease and for a month afterwards.

Before the sulphonamides came into general use a considerable proportion of cases of bacillary dysentery became chronic. Such cases are now seldom seen. They present most of the features of ulcerative colitis and should be treated accordingly (*vide* p. 332).

Joint effusions should be aspirated and counter-irritant dressings applied.

It is most important that the stools should be examined macroscopically and microscopically throughout the disease, in order that the condition of the colon may be assessed. Everything passed from the bowel must be scrupulously disinfected until repeated cultures prove negative.

AMŒBIC DYSENTERY

Amœbic dysentery is a disease of insidious onset and chronic course, caused by infection of the bowel wall by *Entamœba histolytica*. Secondary or metastatic amœbiasis (principally of the liver) may follow the penetration of the amœbæ into the tissues and their spread by the blood stream.

Ætiology.—*Entamœba histolytica*, in its vegetative or active form, is an amœba about two or three times the size of a polymorphonuclear leucocyte. It possesses the power of amœboid movement, of throwing out pseudopodia which engulf the red blood cells, leucocytes and other debris on which it lives, and of secreting a histolysin which enables it to penetrate the tissues. In this form it is extremely delicate and would soon perish when passed from the bowel. In unfavourable conditions it therefore encysts, and the round quadrinucleate cyst thus formed possesses sufficient resistance to allow it to be transferred by the agency of " carriers," flies, water, uncooked food and possibly dust, to be ingested by other persons in whose intestine it excysts and liberates the active pathogenic amœba.

There are other amœbæ and their cysts (notably *E. coli*) which occur in

the intestine and fæces which are liable to be mistaken for *E. histolytica*, but none are pathogenic.

Pathology.—The amœbæ dissolve their way down through the mucosa, submucosa, and muscular layers where they produce small submucous abscesses, so that the mucous membrane becomes studded with minute yellow pustules. These little abscesses burst and produce ulcers which increase in size and become funnel-shaped, the edges being regular and the bases covered with sloughs. These ulcers may coalesce and tend to spread in the long axis of the gut. They are separated by areas of normal mucous membrane. Deeper penetration by the amœbæ may result in perforation, peritonitis, and adhesions between adjacent coils of gut or between gut and liver or spleen. Erosion of blood vessels may cause hæmorrhages and thromboses and the spread of amœbæ to distant parts of the body with resultant metastases. Amœbic ulceration is commonest in the cæcum, hepatic flexure, and sigmoid colon, the lower ileum being only rarely affected. There is general compensatory thickening of the gut. Ulceration may become chronic and be followed by polyposis and carcinoma.

Signs and Symptoms.—The incubation period is several weeks. The onset is insidious, and often there is no more than colic and perhaps mild diarrhœa, indeed death may result from perforative peritonitis, or metastatic amœbiasis may occur without there having been any dysenteric symptoms. Tenesmus is not marked unless the rectum is affected, and abdominal tenderness is localised and may simulate appendicitis. The stools are rarely numerous and consist of fæces flecked with mucus and streaked with blood. They are offensive and are said to resemble anchovy sauce. There is seldom any fever or toxæmia. While gangrenous fulminating cases do occur, the disease typically runs a chronic course which often does not keep the patient to his bed or even away from his work, indeed in the most insidious cases the symptoms may be so slight that the suspicion of malingering may arise, the patient being listless and tired and showing nothing clinically beyond a mild tachycardia and an occasional extrasystole. The seriousness of amœbic dysentery lies not in the dysentery but in the penetrative power of the amœbæ and the dangers resulting from it.

Diagnosis.—Microscopic examination of the stools and the finding of *E. histolytica* or its cysts can alone supply a conclusive diagnosis. For this purpose *warm freshly passed stools* should be repeatedly examined. Often the detection of the amœbæ is facilitated by taking a saline purgative such as 2 drachms of sodium sulphate first thing in the morning. The stool passed afterwards is examined forthwith.

Entamœba coli is not infrequently present in the stools in cases of bacillary dysentery. It is therefore imperative that the pathologist should be competent to distinguish with certainty between these two amœbæ and their cysts. The points of differentiation are beyond the scope of this book and can be learned only by the study of fresh specimens, but it may be said briefly that *E. histolytica* is generally smaller and more active than *E. coli*, and while the former often contains ingested red blood cells, the latter never does. The cysts also tend to be smaller in the case of *E. histolytica* and typically contain four nuclei in that species, whereas the cysts of *E. coli* contain more than four nuclei. Microscopical examination of amœbic stools will also reveal that the red cells tend to show rouleaux formation while comparatively few pus cells and macrophages are seen.

but there are numerous motile bacilli and often a number of Charcot-Leyden crystals.

Sigmoidoscopic examination is of great help in enabling the condition of the bowel to be studied, and amœbæ may often be found in scrapings from the ulcers when it has not been possible to find them in the stools. The comparative painlessness of sigmoidoscopy in amœbic infections is in marked contrast to the pain caused when the operation is performed in cases of chronic bacillary dysentery.

Amœbic dysentery is usually accompanied by a moderate leucocytosis.

Treatment.—There are several drugs that are specific against *E. histolytica*, and all of them possess toxic properties. If laboratory facilities exist, their use as diagnostic agents is therefore to be avoided. Of these drugs emetine, an alkaloid of ipecacuanha, is the most lethal to the amœbæ and the most toxic to the patient.

In acute cases the treatment should follow the general lines recommended for bacillary dysentery, but a single daily saline is usually advisable and the diet may be rather more generous. Emetine hydrochloride 1 gr. in 1 c.c. of distilled water should be given hypodermically on each of the first seven days. It should be remembered that emetine is a dangerous remedy for a serious disease and that it may affect the heart and occasionally the nervous system and the patient must, therefore, be *confined to bed* and carefully watched and nursed.

The patient should then have a course of emetine bismuth iodide (E.B.I.). Owing to its tendency to cause nausea and vomiting, E.B.I. should be given last thing in the evening when the patient is going to remain undisturbed. Ten to fifteen minims of chlorodyne or tinct. opii given half an hour previously may check excessive vomiting. E.B.I. should be administered in gelatine capsules in a dosage of 1 gr. on the first day, 2 gr. on the second day, and 3 gr. on each of the subsequent ten days. During this course colonic lavage should be given daily with a pint and a half of warm water containing 90 gr. of sodium bicarbonate and should be followed by an enema of 6 to 8 oz. of $2\frac{1}{2}$ per cent. chiniofon [1] (B.P.) *which should be retained for eight to ten hours.* The rationale of this treatment is that while emetine acts on amœbæ in the tissues, E.B.I. and chiniofon act on those in the lumen of the bowel.

In resistant or relapsing cases trial should be made of stovarsol (acetarsol) or carbasone in doses of 4 gr. twice daily for ten days, or diodoquin in 3 gr. doses t.d.s. for three weeks. Although it has no action on the amœbæ, penicillin is often beneficial in these cases, presumably by cleaning up secondary infection.

Diet should be light and milk is not contraindicated. Alcohol must not be allowed.

Scrupulous care must be taken to disinfect the stools until repeated examinations fail to reveal amœbæ or cysts. For some time after apparent cure the stools should be periodically examined to make sure that the patient does not become a "carrier" or cyst-passer who will be a danger to the community and liable to develop any of the various amœbic metastases.

Because the diagnosis between bacillary and amœbic dysentery is of such supreme importance and because confusion has in the past so often led

[1] Yatren: quinoxyl, quiniosulphan.

to unnecessary loss of life, the main points of distinction are summarised below :—

Bacillary Dysentery	*Amœbic Dysentery*
An acute, epidemic, febrile disease of short duration and sudden onset occurring most commonly in dry climates and having an incubation period of not more than a week.	A subacute or chronic, endemic, afebrile disease of long duration and insidious onset occurring most commonly in humid climates and having an incubation period of three to twelve weeks.
The tongue is clean, toxæmia is marked, and tenesmus common. There is general abdominal tenderness.	The tongue is dirty, toxæmia is not marked, and tenesmus is unusual. There is localised abdominal tenderness.
The stools are scanty, numerous, odourless, alkaline, and consist almost entirely of blood and mucus—"red-current jelly." Microscopically red blood cells and polymorphonuclears are numerous, macrophage cells are plentiful, and organisms scanty and consist mainly of non-motile bacilli.	The stools are large, not very numerous, offensive, acid, and consist of fæcal material streaked with blood and mucus—"anchovy sauce." Microscopically red blood cells occur in clumps, polymorphonuclears are damaged, macrophages are not common. Charcot-Leyden crystals are often seen and there are numerous motile bacilli.
Leucocytosis is unusual.	Leucocytosis is the rule.
Ulcers, when present, are shallow, with serpiginous outline, the bases consisting of granulation tissue. They tend to occur on the free edges of the transverse folds of the gut. The whole mucous membrane is hyperæmic or necrosed.	Ulcers are deep and funnel-shaped with a regular outline, the bases consisting of sloughs. They occur in the long axis of the gut. Intervening mucous membrane is normal.
The only important complications are arthritis and iritis. Chronic colitis and stenosis may follow.	Apart from immediate dangers such as perforation, peritonitis, and hæmorrhages, the only common complication is hepatitis and liver abscess.

Metastatic Amœbiasis

During the course of amœbic infection of the intestine, invasion of the skin around the anus may occur, and the same thing may happen round a colostomy or appendicectomy wound resulting in a spreading ulceration. Such conditions respond readily to emetine. The true metastatic lesions resulting from the primary infection of the gut are, however, blood borne. The erosion of a small vessel in the gut wall results in the amœbæ being carried up the mesenteric and portal veins to the liver, which is by far the commonest site of such lesions. Amœbiasis of the lung, brain, and spleen may occur.

Amœbic Hepatitis and Liver Abscess

The great majority of untreated cases of metastatic amœbiasis take the form of an abscess, more often single than multiple, in the right lobe of the liver, though early diagnosis and treatment may arrest the condition in the stage of hepatitis which precedes it. The disease is rare in natives and in European women and children.

It should be remembered that although there is always a primary infection of the gut this may have caused such mild symptoms that no history of dysentery is obtainable, and the absence of such history must never cause the possibility of hepatic amœbiasis to be overlooked in any case of debility or chronic ill-health in a person who has lived in the tropics. The condition may arise as long as twenty years after the primary infection.

Symptoms, Signs, and Diagnosis.—The existence of malaise, irritability, loss of weight and appetite, coated tongue, and irregular action of the bowels in one who has lived in a country where amœbiasis is endemic should never

fail to arouse suspicion. If to these symptoms be added a muddy complexion, evening pyrexia and night sweats, heaviness or pain in the right hypochondrium and a dry irritative cough, the diagnosis can hardly be in doubt. Pain may be referred to the right shoulder or to the appendicular region, and physical examination may show enlargement of the liver and signs of pleural involvement or right basal pneumonia. Diminution of movement of the diaphragm and deformity of its right dome may be seen in radiographs, and when accompanied by a moderate leucocytosis with a relatively normal lymphocyte : polymorphonuclear ratio, it is presumptive evidence of the existence of a fully developed abscess which may be confirmed by aspiration. Amœbæ, though present in the growing edge of the abscess, are not often found in the " pus."

Sufficient thought must be given to differential diagnosis to prevent the possibility of overlooking hepatic enlargement due to malaria, hydatid cyst, gumma, malignant disease, and kala-azar, but exploratory puncture is generally a justifiable confirmatory measure. In acute cases with congestion it may be advisable to postpone this step until a course of emetine has failed to reduce the temperature and the leucocytosis. Aspiration should be performed under local or general anæsthesia with a wide bore cannula and ample suction, the site of election being, in the absence of localising signs, a point in the eighth or ninth intercostal space in the anterior axillary line. The needle should be introduced inwards and slightly upwards and backwards for a distance of three to three and a half inches. Several punctures should be made before abandoning the attempt. The stools should always be carefully and repeatedly examined for amœbic cysts.

If untreated, an amœbic abscess may burst into the lung, pleura, pericardium, or peritoneum, or may become secondarily infected Adequate treatment reduces the mortality from about 70 per cent. to practically *nil*.

Treatment.—In amœbic hepatitis a course of ten daily hypodermic injections of 1 gr. of emetine should be given during which the *patient must be kept in bed* on a low diet. If cysts are present in the stools this should be followed by a course of emetine bismuth iodide by the mouth and chiniofon enemata as in amœbic dysentery.

Even when an abscess has formed, emetine alone may often effect a cure, but as a considerable amount of " pus " may be present (as much as 6 pints has been recorded) aspiration may be necessary in association with a course of emetine. After aspiration, 1 or 2 gr. of emetine in 10 c.c. of sterile distilled water may be injected into the abscess cavity. Aspiration may have to be repeated if the cavity fills up again. Strict attention to asepsis must be observed or secondary infection will inevitably follow. Surgical drainage is to be avoided and open operation is rarely justified.

CHOLERA

Ætiology and Epidemiology.—The disease is caused by the comma-shaped *Vibrio choleræ* which infects the mucosa of the small intestine and produces a potent endotoxin. The vibrio is usually ingested in water contaminated by persons suffering from the disease or carrying the organism during convalescence. Healthy carriers are rare. Less commonly the disease

is contracted by eating food (especially raw fruit or vegetables) which in turn has been contaminated by water, a carrier, or flies. India is the endemic focus from which the disease spreads along the routes taken by traders and pilgrims to all parts of Asia. It is now well over half a century since the disease occurred in the British Isles or America. Although a certain minimum atmospheric humidity is necessary, the spread of an epidemic depends chiefly on the existence of insanitary conditions, and it is to the eradication of these conditions that Western Europe owes its comparatively new-found freedom from the disease.

Pathology.—The multiplication of the vibrio in the small intestine and the liberation of toxins cause a hyperæmia and, later, a superficial necrosis of the mucous membrane and the loss of large quantities of fluid from the bowel. Severe depletion of water and salts ensues causing hæmo-concentration, lowering of blood pressure, suppression of urine and uræmia, muscular cramps, and acidosis. These effects are aggravated by the action of the absorbed toxins which themselves cause a fall in blood pressure and damage to the secreting tubules of the kidneys.

Signs and Symptoms.—After an incubation period which varies from a few hours to about a week, and with or without premonitory diarrhœa, the disease sets in with the passage of profuse and frequent motions often accompanied by colic. The motions, at first fæcal, rapidly lose their colour and assume the typical "rice water" appearance—watery fluid containing flakes of necrosed intestinal epithelium. In this, the *stage of evacuation*, enormous quantities of this fluid are lost both by diarrhœa and vomiting. As the fluid contains the vibrio the attendants run a considerable risk of being infected. Dehydration produces intense thirst, the urine diminishes in amount, the blood pressure falls, the pulse becomes small and thready, the temperature drops (although the rectal temperature may be normal or even considerably raised), and the patient passes into the *algid stage*. The eyes are sunken, the intra-ocular tension is reduced, and the eyelids pearly white. The skin becomes clammy and wrinkled ("washer-woman's fingers") and of an earthy hue, often with cyanosis at the extremities. The surface temperature and the blood pressure drop still further and the pulse may be barely perceptible. Severe and agonising cramps in the calves occur, and the patient, though fully conscious, cannot speak above a husky whisper. The urine may be completely suppressed. If a vein be opened only a small bead of dark tarry blood may exude. It is in this stage, often within twenty-four to thirty-six hours of the onset of the disease, that death is most likely to occur either in coma or after sudden collapse.

Recovery is heralded by a general remission of symptoms which constitutes the *stage of reaction*. The motions decrease in number and volume, and bile reappears in them. The temperature rises and may become hyperpyrexial, the pulse improves, urine is secreted, and the skin regains its normal appearance. Recovery is usually surprisingly rapid having regard to the seriousness of the disease, but in this stage the patient is by no means out of danger, and death may occur from pneumonia, hyperpyrexia, or uræmia. Convalescence is apt to be complicated by anæmia, toxic nephritis, chronic enterocolitis, furunculosis, insomnia, and mental depression.

In addition to the classical cholera described above, ambulatory cases may occur (especially late in an epidemic), and may suffer from little more than malaise and diarrhœa. On the other hand, severe, fulminating cases

are sometimes seen in which death from toxæmia occurs before diarrhœa or vomiting have made their appearance, the so-called "cholera sicca."

Mortality in treated cases varies from 20 to 50 per cent.

Diagnosis.—This rests finally on the demonstration of *Vibrio choleræ* in the evacuations by cultural methods. Once an epidemic is well established diagnosis presents no difficulty, but in the earlier or sporadic cases bacillary dysentery, malignant malaria, and food poisoning must be excluded. In malaria the temperature is high, and in food poisoning the vomiting precedes the diarrhœa, whereas in cholera it follows it. It should be remembered that dysentery, enteric fever, or malaria may coexist with cholera.

Treatment.—This aims to replace fluid and salt lost and to destroy toxins.

Throughout the disease the temperature must be carefully watched and the urine must be measured. The patient must be kept warm and should wear a "cholera belt." Food should be withheld altogether until the choleraic diarrhœa ceases, but unlimited boiled water "pinked" with potassium permanganate (3 gr. to the pint) should be allowed, and potassium permanganate in pill form should be administered until the stools become and remain green. As much as 50 gr. may be given in the twenty-four hours to oxidise the toxins. Kaolin in a strength of 1 to 3 in water may be swallowed in large quantities and acts by adsorbing the toxins. To check purging and vomiting it is wise to give, from the outset, eight or nine half-hourly doses of essential oils—clove, cajaput, and juniper, 5 minims of each, with 30 minims of spt. æther. and 15 minims of acid sulph. arom. Bacteriophage and antitoxic serum, although somewhat uncertain in their action, are worth a trial, but they must be given immediately symptoms appear.

The essential treatment in cholera, however, is the *replacement of fluid and salts*. This should be effected by the slow intravenous infusion of two solutions of saline—one alkaline, the other hypertonic. The alkaline solution consists of 90 gr. of sodium chloride and 160 gr. of sodium bicarbonate in a pint of sterile distilled water. The hypertonic solution consists of 120 gr. of sodium chloride, 6 gr. of potassium chloride, and 4 gr. of calcium chloride to the pint. One pint of the alkaline solution is followed by as many pints of the hypertonic solution as are indicated by the degree of dehydration as judged clinically and by estimations of blood pressure and hæmoglobin. If these special solutions are not available three or four pints of normal saline should be given. Infusion may need to be repeated if the blood pressure remains low or collapse still threatens. If there is anuria a pint of normal saline should be given by the rectum every two hours, and fomentations should be applied over the loins.

The hypodermic injection of drugs is to be avoided in the algid stage as they are liable to have a dangerous cumulative effect when the circulation improves during the stage of reaction, but pituitrin, digitalin, atropine, or adrenaline may be necessary to combat severe collapse or anuria. Cramps may be relieved by massage, warmth, or short chloroform inhalations.

In the stage of reaction bismuth salicylate in 15 gr. doses may control continued purging. Convalescence must not be hurried and diet must be increased with the greatest care.

Prophylaxis.—*Personal.*—Inoculation with cholera vaccine gives a reasonable degree of protection for a few months. All water used for drinking or in the preparation of food should be boiled or chlorinated. Vegetables

and fruit eaten raw should be thoroughly disinfected or avoided altogether. Care should be taken to avoid anything likely to upset the digestive tract, not excluding purgatives.

General.—Cholera patients must be isolated for six weeks or until the stools are free from the vibrio, and during this time all dejecta as well as all soiled clothes or bed-linen must be thoroughly disinfected. Carriers should be sought out and contacts isolated for ten days.

Water supplies must be carefully supervised and some sure method of sterilisation practised. Access of flies to infected material and to food must be prevented.

SPRUE

Sprue is a chronic disease of variable symptomatology, but in typical cases dyspepsia, abdominal distension and diarrhœa, glossitis, and anæmia are present. It occurs in those who live or have lived in certain tropical or subtropical areas, especially India and Ceylon, China, the East and West Indies, and Central America. It bears a close relationship to cœliac disease and idiopathic steatorrhœa (which has been called " non-tropical sprue ").

Sprue is probably a deficiency disease, the essential fact in the ætiology being impairment of absorption from the small intestine consequent on atrophy of the mucous membrane. The cause of this atrophy is not known and is the subject of much speculation. The impairment of absorption embraces fats, glucose, calcium, iron, vitamins, and the extrinsic anti-anæmic factor. A consideration of the results of the failure to absorb these substances will explain the symptoms.

Symptoms are insidious in onset and follow an uncertain but prolonged incubation period. Only in fully developed cases are all the symptoms likely to be seen, and, moreover, their severity varies greatly. Irritability, flatulent dyspepsia, and morning diarrhœa are among the earliest manifestations. The stools are large, pale, gaseous and foul smelling, and may contain twice the normal proportion of fat, which is, however, completely split. Soreness of the tongue with thinning of the mucous membrane and atrophy of the filiform papillæ is a common and distressing feature. Meteorism, cramps, and tetany may occur, and a megalocytic anæmia may develop which is indistinguishable from true pernicious anæmia. There may be achlorhydria but rarely a complete achylia. In late cases peripheral neuritis and signs of subacute combined degeneration of the cord may appear, and in untreated cases death follows increasing debility and emaciation.

Treatment.—There is no specific remedy. The object of treatment must be to give complete bodily rest and to administer small frequent feeds of only the most easily absorbed substances. Fats and fermentable carbohydrates must, therefore, be reduced to a minimum. A milk or high protein diet should be given with parenteral administration of liver extract until the condition of the patient and the constitution of the stools indicate definite improvement. Fruit, meat juice, and liver may be added gradually, but the diet must be carefully regulated for at least six months after apparent cure. Although vitamin therapy has not yet emerged from the experimental stage it is a logical treatment, and excellent results have been obtained from large doses of the B complex (nicotinic acid and riboflavin). The anæmia should respond to intramuscular injections of liver extract and the administration

of iron. Folic acid in doses of 20 mg. daily for three or four weeks has proved effective in controlling diarrhœa and improving the appetite, but its effect on anæmia and fat absorption is doubtful. In very advanced cases blood transfusion should be tried. Strict but sympathetic nursing is essential, and the patient should leave the endemic area as soon as possible.

YELLOW FEVER

Yellow fever is a severe, acute, specific disease caused by a filterable virus transmitted from man to man by the mosquito *Aëdes ægypti*. It is characterised by fever, albuminuria, hæmorrhages, jaundice, and its peculiarly limited geographical distribution. It is a disease that is becoming increasingly important epidemiologically as the endemic foci become the junctions for more transcontinental air traffic.

Ætiology and Epidemiology.—The virus circulates in the blood of cases of yellow fever only during the first three days of the disease. During this period the virus may be taken up by the mosquito which is capable, after an interval of about ten days, of transmitting it to susceptible persons in whom the disease develops after an incubation period rarely exceeding five days. In this way epidemics are liable to occur whenever *aëdes* mosquitoes and susceptible persons exist in sufficient numbers. In the meantime, however, the disease is kept alive in the form of sporadic and often unrecognised cases among natives. In forest areas of South America and Africa the disease exists in a " jungle " form in certain animals amongst which it is transmitted by various forest mosquitoes. From this reservoir man may at any time become infected if he happens to be bitten by such an infected forest mosquito. In urban districts the disease does not occur in the absence of *aëdes* mosquitoes. These are found all over the tropical and subtropical world, and yet yellow fever is confined to limited areas in South America and tropical Africa. The spread of the virus to other parts of the world (especially India), where the vector and susceptible populations await it, might well precipitate the most calamitous epidemic the world has ever seen. With the development of rapid air and overland transport by which many thousand miles can be covered within the incubation period, this risk has been greatly increased, and to meet it the strictest quarantine laws have been applied at ports and aerodromes, and elaborate steps have been taken to prevent the virus being exported or imported in man or mosquito.

Control of yellow fever depends on the immunisation of all persons entering or living in an endemic area, the quarantine of all non-immunised persons leaving such areas, the prevention of the export of mosquitoes in sea, land, or air transport, the early recognition and screening of cases of the disease and the local elimination of *aëdes* mosquitoes. Since these mosquitoes are domestic in their habits and breeding places their destruction is not difficult and involves attention to tanks, gutters, tins, flower vases, and other collections of stagnant water in which they breed and the use of insecticidal sprays (especially D.D.T.) in native houses.

Inoculation with a living virus vaccine should be given to everyone at risk. Immunity follows within a fortnight and lasts for at least four years. Mosquito nets should always be used.

Pathology.—There is jaundice and evidence of widespread hæmorrhages, especially of the stomach and bowel, and generalised fatty degeneration of the organs and vessels. The liver is friable and of a "box-wood" colour, fatty and hyaline degeneration is marked at the periphery of the lobules, and there are diagnostic changes in the nuclei and cytoplasm of the liver cells.

Signs and Symptoms.—Onset is sudden and there is often a rigor. For two or three days there is fever with general congestion, frontal headache, vomiting, epigastric and loin pain, and a full rapid pulse. By the second day, *albumin appears in the urine in increasing quantities*. The temperature may then fall with general abatement of symptoms. Convalescence may commence at this stage, but more often a stage of reaction ensues in which the urine diminishes and albuminuria increases; hæmorrhages (especially of the stomach and bowel, causing black-vomit and melæna) occur. Jaundice usually appears by the third day. The pulse tends to be slow in relation to the temperature (Faget's sign). In fatal cases toxæmia increases and death occurs in coma or convulsions. Abortive, ambulant, severe, and pernicious types are described. Mortality is about 25 per cent.

Diagnosis can be made with absolute certainty only by animal inoculation. Clinically the increasing albuminuria and falling pulse-rate should arouse suspicion. Jaundice and black-vomit must not be relied upon as they are usually late features. In spirochætosis icterohæmorrhagica there is a leucocytosis, whereas a leucopenia usually accompanies yellow fever. Malaria, blackwater fever, relapsing fever, and dengue may bear a close resemblance. Post-mortem diagnosis by the histological appearance of the liver may be of great epidemiological value in doubtful or sporadic cases.

The mouse protection test has been of supreme value in revealing areas where yellow fever is or has been endemic. The test depends on the fact that the blood of an individual who has had the disease contains immune bodies which protect a mouse when injected with a dose of virus that would otherwise prove fatal. By noting the age above which the members of an isolated community show positive protection tests it is possible to say when an epidemic last occurred. By this means, too, the existence of "jungle" yellow fever has been demonstrated in man and animals in areas where *aëdes* mosquitoes do not exist. The test is of no diagnostic value during the attack as it becomes positive only during convalescence.

Treatment is symptomatic, there being no known specific. Careful nursing is essential. Alkaline fluids and glucose both by the mouth and intravenously are given to combat the toxæmia and uræmia. The patient must, of course, be kept under a mosquito net.

DENGUE

Dengue is a specific fever caused by a virus conveyed by the yellow-fever mosquito *Aëdes ægypti*. The disease, which lasts about a week, is apt to occur throughout the littorals of the Middle East and elsewhere in epidemics or pandemics, and is distinguished by "saddle-back" temperature chart, skin rash, and severe rheumatic-like pains ("break-bone fever").

The blood of the patient is infective to the mosquito for a day before the onset of symptoms and for the three following days. The mosquito

becomes infective ten to fourteen days after feeding on a dengue patient. The incubation period is five to nine days.

Symptoms.—The onset is sudden with fever, congestion of the skin, supra- and post-orbital pain, suffusion of the conjunctivæ, and severe pains in the limbs, loins, and back. After two or three days the temperature falls and the patient feels much better, but after one or two days the fever and pains return and the typical rash appears on the hands, limbs, and trunk. It consists of circular, slightly raised, reddish-brown rubeoloid spots which coalesce to give an appearance " midway between scarlet fever and measles." This terminal fever and eruption rarely last more than twenty-four hours. Bradycardia and leucopenia with relative lymphocytosis are present throughout the disease, which is often followed by general debility, mental depression, insomnia, furunculosis, and an immunity of uncertain duration. Mortality is *nil*.

Treatment is symptomatic. The patient must be kept in bed under a mosquito net until the temperature is normal and the rash has subsided. Morphia may be necessary to lessen the pains.

Prevention can be effected only by the use of mosquito nets and the extermination of *aëdes* mosquitoes by swatting and spraying and attention to all potential breeding places.

PHLEBOTOMUS (" SANDFLY ") FEVER

Sandfly fever is a short specific fever caused by a virus transmitted by a midge of the genus *Phlebotomus*. It occurs in most tropical and subtropical countries, but especially on the Mediterranean littoral.

Symptoms.—Incubation period is about five days. Fever usually lasts three days and is accompanied by congestion, aching pains in the back and legs and severe frontal and post-orbital pain with photophobia. A leucopenia gives place to a moderate leucocytosis when the fever subsides.

Treatment is symptomatic. The patient must be kept in bed under a sandfly net, and opium or Dover's powder should be administered. There is no mortality, but convalescence is apt to be slow.

Prevention depends on the avoidance of sandfly bites by the use of nets of very fine mesh and suitable clothing after dark, and on the destruction of sandflies and their breeding places. D.D.T. has proved particularly effective against sandflies.

TYPHUS FEVER

Typhus fever is really a group of fevers all of which are caused by infection with *Rickettsia*, a pleomorphic virus visible with a high-power microscope, which is present in the blood during the first few days of the disease. Typhus fever can be broadly divided into two main types : the classical epidemic typhus which is transmitted by lice from man to man, to which fact it owes its epidemic character and its cosmopolitan distribution ; and endemic typhus, primarily a disease of animals which is accidentally transmitted from them to man by ticks, fleas, or mites, and which is localised in various parts of the world where the animal reservoir of infection, the vector, the

climate, and other local peculiarities modify the clinical manifestations of the disease.

Epidemic Typhus.—This louse-borne disease is associated with war, famine, and destitution, which cause populations to neglect personal cleanliness and to crowd together for warmth or safety, thus providing conditions ideal for the spread of infected lice. It is a disease not of hot climates but of lousy populations, and is most common in China, North Africa, and Eastern and South-eastern Europe.

The incubation period is from five to fourteen days. Prodromal headache and malaise lasting one or two days usually precede a sudden rise of temperature to 103° or 104° F. with congestion, suffused conjunctivæ, and dry, furred tongue. The marked degree of prostration occurring within the first few days of the disease, with a typical vacant expression, are the result of severe toxæmia, and are of diagnostic importance. About the fifth day a rash appears on the abdomen and chest, and spreads to all parts of the body except the face, which is generally spared. The rash is variable in appearance, but typically shows roseolar macules superimposed on subcutaneous petechiæ or mottlings. This rash is the result of necrosis of small blood vessels which occurs in the viscera and brain as well as in the skin. With the appearance of the rash there is an exacerbation of symptoms. Headache becomes severe, the tongue is dry and brown, toxæmia increases, and the " typhoid state " ensues so that the patient becomes feebly delirious or comatose with albuminuria, retention of urine, and enlargement of the spleen. By the twelfth or fourteenth day the temperature falls by crisis or rapid lysis, and recovery ensues or deepening coma ends in death from heart failure. Complications are not common, but hypostatic pneumonia, venous thrombosis, and gangrene may occur, and myocarditis may persist into convalescence. Mortality varies between 5 and 50 per cent. in different epidemics, and is greatly increased by debility and advancing age.

Brill's Disease, occurring in America, is thought to be a mild recrudescence of epidemic typhus in persons who have previously suffered from the disease or, at least, lived in endemic areas. It is apparently not transmitted by lice or any other arthropod.

Trench Fever is a louse-borne rickettsial disease resembling much attenuated typhus, which was first described during the 1914-18 war.

Diagnosis.—In sporadic cases the early prostration and stupor should arouse suspicion, while the rash should confirm it. In epidemics the diagnosis is unlikely to be in doubt. The Weil-Felix reaction, which becomes positive by about the fifth day and remains so for some months, is of great assistance. It depends on the fact that the serum of a typhus patient agglutinates *Bacillus proteus* and that different serological variants of the bacillus are constantly agglutinated in the different types of the disease. The organism, although it can frequently be isolated from cases of typhus, has not been shown to be any more than a concomitant and causes no specific immune bodies to be formed, though such bodies are produced by inoculation with *B. proteus*. Complement fixation tests are in use employing rickettsial antigens.

Endemic or Zootic Typhus is a group of diseases which includes :—

Flea-borne typhus, urban or " shop " typhus of Malaya, ship fever of the Mediterranean and murine typhus of many other parts of the world. The causative organism is serologically closely related to that of epidemic typhus

but is less virulent in man. Although it is normally transmitted from rats and occasionally from dogs by fleas, there is some evidence that it is transmissible, in favourable circumstances, from man to man by lice and that it may thus become epidemic.

Tick-borne typhus, Rocky Mountain spotted fever of North America, Marseilles fever and tick fevers of India, Africa, South America, and Australia. The causative organism is variable in its serological reactions. Small rodents and dogs form the animal reservoir.

Mite-borne typhus, Japanese river fever, rural "scrub" typhus of Northern Australia and the Far East, and mite typhus of India and Burma. The causative organism belongs serologically to a group distinct from the flea- and louse-borne type but related to it. It is transmitted from field mice and rats by larval mites which infest vegetation at certain times of the year. The disease therefore tends to be localised to grassy and wooded country.

In these diseases the symptoms vary considerably but are usually much milder than in epidemic typhus and the prognosis is better. Mite typhus may be severe, however, and often there is local necrosis at the site of the bite because the mite remains buried in the skin. The rash is often profuse in tick typhus and slight or absent in flea and mite typhus.

Treatment is mainly a matter of careful nursing. No specific drug is known. The hygiene of the mouth is important and cardiac stimulants are usually necessary.

Prevention depends on keeping the body and clothes free from lice or on avoiding the bites of fleas, ticks, and mites. D.D.T., blown into the clothes and hair as a 5 to 10 per cent. powder or used in solution to impregnate clothing and bedding, has revolutionised the control of epidemic typhus. The disinfection of clothing and bedding by heat still has its place, however, because D.D.T. is only an insecticide and does not kill rickettsiæ which may be present and infective in the dried fæces of lice. The periodical impregnation of clothing with dibutyl phthalate or benzyl benzoate will protect the wearer against mites.

There is little risk of a serious epidemic of typhus occurring in a well-fed population.

Various rickettsial vaccines are in use and serve as a subsidiary measure of control.

RELAPSING FEVER

Relapsing fever is an acute specific infectious disease characterised by sudden onset, high fever lasting for a few days and sudden defervescence by crisis. During the febrile period headache, enlargement of the liver and spleen and leucocytosis, and often an erythematous rash, which spreads downwards from the neck, are present. Sweating and diarrhœa usually accompany the crisis. Relapses occur, but the duration of both the pyrexial and apyrexial periods varies considerably, the symptoms tending to become milder. Mortality is usually below 5 per cent., but may be much higher. The disease is caused by a spirochæte (*S. recurrentis*), demonstrable in blood smears during the pyrexial periods only, and transmitted by lice and by ticks.

Louse-borne relapsing fever may occur wherever lice are found, and therefore depends more on personal hygiene than on climatic conditions for its

existence, becoming epidemic in times of war and famine. It is endemic in India, China, and Eastern Europe. There are usually two or three relapses, each lasting about a week, separated by apyrexial periods of the same duration. Prevention is dependent on personal cleanliness and on the destruction of lice and their eggs.

Tick-borne relapsing fever occurs in many tropical countries, especially Central and West Africa, North-west India and Iran, Spain and Morocco, California and Panama. It is a " place " disease, and is most commonly contracted in native rest-houses, the tick being parasitic only while it feeds, thereafter dropping off and living in crevices in walls or in the ground. This form of the disease therefore remains localised, is little affected by season, and never becomes epidemic. The tick-borne type is, on the whole, more severe than the louse-borne, the febrile periods are shorter, the relapses more numerous, and the disease is more resistant to treatment and more likely to be followed by nervous complications. Prevention depends on the avoidance of tick-infested sites and of their bites.

Treatment.—Intravenous neoarsphenamine should be given early in the pyrexial stage. A single dose of 0·45 gm. often effects a complete cure. Penicillin, even in very large dosage, has not proved any more effective than neoarsphenamine.

PLAGUE

Plague is an acute specific disease which occurs in epidemic form in tropical countries. The main endemic foci are in India and China. Severe epidemics have occurred in Europe (as, for instance, the Great Plague of London), but are now practically limited to Asia and South America.

The disease is primarily an epizootic of rats and other rodents, and is caused by the *Bacillus pestis*. When rats contract the disease the fleas with which they are infested take up the bacilli from the rats' blood. When the rats die of plague the infected fleas leave their bodies and seek other warm-blooded animals on which to feed, and thus man becomes infected. Rats, therefore, form the reservoir of the disease, and a sudden heavy mortality among rats should be a warning of an impending human epidemic. In endemic areas and during epidemics rats found dead should never be touched or approached closely but should be shovelled into cresol or oil and subsequently examined in the laboratory for the presence of *B. pestis*.

Signs and Symptoms.—The incubation period is from two to five days. There are three clinical types of the disease in all of which there is marked toxæmia with fever, headache, and drowsiness.

Bubonic plague is characterised by inflammation and enlargement (buboes) of those lymph glands which lie in the course of the lymphatics draining the site of the flea-bites. Inguinal buboes are the rule, while axillary and submaxillary infections are rare. They are exquisitely tender and frequently suppurate. *B. pestis* can be obtained by gland puncture. Mortality varies from 20 to 90 per cent.

Pneumonic plague is transmitted by direct droplet infection from man to man and not by fleas. The physical signs are those of a patchy broncho-pneumonia with blood-stained sputum which teems with the bacilli. It is almost invariably fatal within a few days.

Septicæmic plague results from the entrance of large numbers of highly

virulent bacilli into the blood, and is almost always fatal before the lymph glands have time to enlarge.

An ambulant form (pestis minor) is described, which may go unrecognised and consequently be a source of danger to others.

Diagnosis.—Early cases may closely resemble typhus fever. Buboes must be differentiated from those of venereal origin and from filarial adenitis. Bacteriological diagnosis is a simple matter in all forms of the disease.

Treatment is mainly symptomatic and is unlikely to affect the course of the disease materially. Sulphathiazole is generally considered to be the most useful drug. If available, anti-plague serum should be given early and repeatedly. Penicillin has not proved effective, but streptomycin has been used with success.

Prevention consists in wholesale destruction of rats and the rat-proofing of food and grain stores. Ships require special attention to prevent rats from embarking and disembarking. Cases must be strictly isolated for a month and fomites destroyed or disinfected. The quarantine period is ten days.

Personal prophylaxis involves the avoidance of places where there are likely to be fleas and immunisation with one of the various *B. pestis* vaccines.

LEPROSY

Leprosy is a chronic infective disease characterised by granulomatous lesions of the skin and nerves caused by *Bacillus leprœ* (*Mycobacterium leprœ*). It is endemic in many tropical and subtropical countries, but is prevalent only among primitive peoples. It is acquired by contagion through intimate personal contact over a long period and is not now thought to be hereditary.

Symptoms.—After an incubation period of several years there is prodromal fever of variable severity and duration followed by the appearance of a pleomorphic rash associated with loss of hair, which occurs most commonly on the face, extensor surfaces of the limbs, or the trunk. The " period of specific deposit " follows, during which lepromata (tumours consisting mainly of small round cells and *B. leprœ* and comparable with tubercles in tuberculosis) are formed either in the skin or in the peripheral nerve trunks, or, occasionally, in both situations. In the first instance nodular or skin leprosy results ; in the second, anæsthetic or nerve leprosy. In skin leprosy, brownish, greasy, depilated patches occur which may later coalesce to produce, when the face is affected, the classical " leonine facies," in which the eyes and nasal septum are eventually affected and the leper dies of intercurrent disease. In nerve leprosy the destruction of nerve tissue causes localised hyperæsthesia and anæsthesia, and, later, muscular atrophy, deformities, and trophic ulceration. The disease may persist for many years, being far more chronic than the skin form. *B. leprœ* can be demonstrated by the methods applicable to *B. tuberculosis* in smears made from the nasal discharge or the contents of the lepromata.

Treatment.—Apart from attention to general health and hygiene, which is most important, chaulmoogra or hydnocarpus oil, though not specific, offer the best chance of delaying the progress of the disease. Among the numerous preparations available, sodium hydnocarpate (alepol) is the most generally used, and is administered intramuscularly or subcutaneously in

doses of 1 to 5 c.c. of a 3 per cent. solution. Large doses of potassium iodide are given by mouth. Derivatives of diaminodiphenyl sulphone [1] have recently been shown to exert an inhibitory effect on some lesions. Surgical intervention may be necessary in the treatment of corneal involvement, deformities, and leprotic ulcers. Lepers, especially those with nasal discharge or open sores, should be segregated, and children born of lepers must be separated from them at birth.

YAWS

Yaws is a chronic, contagious, granulomatous disease with many similarities to syphilis (and of which syphilis is possibly a neurotropic form) common in tropical Africa, Malaya, the West Indies, and elsewhere. It is caused by *Spirochœta pertenue* (which is indistinguishable from *S. pallida*), but is non-venereal and is never acquired hereditarily or congenitally. It is commoner in children than adults and in males than females.

Symptoms.—As in syphilis, there are three stages. A primary papule occurs at the site of inoculation and may develop into a fungating granuloma or " yaw " several centimetres in diameter and accompanied by some general constitutional disturbance. Several months later a secondary rash and numerous secondary yaws appear which have probably been spread from the primary yaw by scratching. Yaws resemble raspberries in appearance and have given the disease its synonym " *frambœsia*." In the tertiary stage extensive ulceration, palmar and plantar lesions, and bony deformities may occur, but visceral and nervous manifestations are unknown. The blood gives a positive Wassermann reaction, but the cerebrospinal fluid does not.

Treatment.—Penicillin (1,200,000 units in four days) produces rapid clinical cure but often fails to change the Wassermann reaction. Neo-arsphenamine, preferably combined with bismuth, is also specific.

RABIES

Rabies is a disease chiefly affecting dogs, wolves, and jackals, but occurs also in other animals, including cattle, horses, pigs, and cats. It is due to a neurotropic virus which invades the central nervous system via the peripheral nerves. It is transmitted by the bite of a rabid animal, the saliva of which contains the virus. The disease is common in tropical countries because of the numerous jackals and pariah dogs that are invariably at large there, but it also occurs in the Arctic countries and all over the world, and has been stamped out in Britain only by the strictest quarantine regulations.

Rabies in the dog, because of that animal's highly developed intelligence, produces marked psychical disturbances. The animal becomes morose, irritable, and easily frightened, and the bark changes in character. Later convulsions may occur and the dog crawls away to die. It rarely bites man or other animals unless they interfere with it. Sometimes the disease assumes a paralytic form. It is invariably fatal within ten days.

Rabies in Man.—The incubation period varies with the severity and site of the bite, but is generally between three and twelve weeks. The patient

[1] *e.g.*, promin, diasone, sulphetrone.

becomes depressed, irritable, and hypersensitive to all stimuli. Reflex spasms of the organs of deglutition occur when attempts are made to eat and especially to drink, and have given the disease, as it occurs in man, the synonym "hydrophobia." Maniacal symptoms and paralysis may occur, and, within three days, convulsive seizures give place to a rapidly fatal coma. Occasionally the disease may be paralytic in type from the onset. Consciousness is retained almost to the end.

Treatment.—No treatment is of any avail once the symptoms have developed.

Prophylaxis.—Wild dogs should be destroyed and steps taken to keep pets away from them. In more civilised countries muzzling and quarantine measures should be enforced.

Inoculation with a vaccine of fixed attenuated virus aims at producing immunity during the incubation period and reduces the incidence of the disease in persons bitten by rabid animals from 16 per cent. to less than 1 per cent. Injections are given daily for periods up to twenty-one days according to the method of preparation employed.

Any person bitten by a possibly rabid animal should have the bite cauterised with carbolic or nitric acid and commence treatment immediately. The animal should be securely chained, and if it is still alive at the end of ten days the patient has nothing to fear and may discontinue injections. If it should die or be killed, the brain should be examined for the pathognomonic oxyphilic granules (Negri bodies) which can usually be demonstrated in the ganglion cells of the hippocampus.

EFFECTS OF HEAT

In a hot atmosphere, man must lose heat in order to keep the body temperature within physiological limits. This he does almost entirely by sweating, but sweat can evaporate and cool him only to an extent inversely proportional to the degree of saturation of the surrounding atmosphere. In still, hot air, with a high relative humidity, sweating continues but merely results in great loss of fluid and salt without an appreciable loss of heat. As much as 2 or 3 gals. of fluid containing 1 to 1½ oz. of sodium chloride may thus be lost in twenty-four hours. This may happen not only in the tropics but in any part of the world, as in stokeholds and boiler-rooms, showing that heat from the sun is not an essential causative factor. A wet-bulb temperature above 80° F. is always dangerous.

Heat Cramps of the voluntary muscles are due to loss of sodium chloride. They occur most commonly in stokers and miners doing hard physical work in a hot, still atmosphere. The condition can be prevented and cured by an adequate intake of salt and fluid.

Heat Exhaustion (*Syncope*) occurs in the man who is unacclimatised or whose efficiency is impaired by disease, fatigue, alcohol, overcrowding, or unsuitable clothing. Giddiness and nausea are followed by sudden faintness with or without loss of consciousness. The skin is moist and clammy, the breathing shallow, the pulse thready, and the temperature normal or subnormal. Urine is scanty and the salt content diminished. Treatment consists of fresh air and stimulation followed by rest and replacement of the lost fluid and salt by the mouth or partly by the rectum or parenterally if the

condition is serious. If the condition is neglected, heat stroke is likely to ensue.

Heat Stroke, always a grave emergency, results from the inability of the body to lose sufficient heat by evaporation to an already highly saturated atmosphere or from the failure of the sweating mechanism. This may follow clinical heat exhaustion or, in the fitter or better acclimatised man, may occur without warning. Usually there is some premonitory anxiety and restlessness, headache and frequency of micturition with diminution of urinary chloride. Any existing infection seems to precipitate the condition. The temperature rises rapidly to hyperpyrexial levels, the skin becomes dry and hot, the face congested, the pulse full, rapid, and irregular, the breathing stertorous and the pupils contracted. Delirium, convulsions, and coma ensue, and *unless treatment is given at once the patient will soon die.* He should be put in the coolest place immediately available, stripped, wrapped in a sheet, sprayed with water and vigorously fanned to imitate the natural process of cooling by evaporation of water from the skin. The use of ice or very cold water is relatively inefficient as it causes cutaneous vaso-constriction. The rectal temperature should be taken every five minutes and the treatment stopped when it falls to 102° F. Venesection, lumbar puncture, and artificial respiration may be necessary. *If there is the least possibility of the symptoms being due to cerebral malaria, intravenous quinine must be given immediately.* Once the temperature has fallen, stimulants may be required and the patient must not be allowed to become chilled. Strychnine should be avoided on account of its convulsant effect. He will need close attention for several weeks as he is liable to relapse, and he should be transferred to a temperate climate as soon as he is well enough.

Prevention of heat effects involves suitable housing, ventilation, and clothing, moderation in the consumption of alcohol, avoidance or wise timing of physical exertion and, most important of all, the replacement of the salt and fluid lost in the sweat. In every case of serious illness in a hot climate the output of urine and its salt content should be measured and recorded in order that the onset of heat stroke or heat exhaustion may be anticipated. A minimum daily output of 50 oz. (1,450 c.c.) is desirable with at least 6 gm. of sodium chloride per litre.

The sun may cause glare and sunburn and may light up a dormant pulmonary tuberculosis, but its direct rays on any part of the body (*e.g.*, the head) cause no other symptoms, provided adequate dissipation of heat is maintained from the body as a whole.

F. E. Lipscomb.

DISEASES DUE TO METAZOAN PARASITES

DISEASES DUE TO FLUKES

TREMATODES or flukes, a number of which are parasitic in man, have a leaf-shaped unsegmented body equipped with suckers. Only one variety is important in the production of disease in man, the Bilharzia (Schistosoma), which produces bilharziasis.

Life History.—There are numerous varieties of flukes which infest man, and the habitat of the adult may be in the intestine, the bile-ducts, the lung, and the blood vessels. Fertilised eggs are discharged in the fæces, the urine, or the sputum ; these eggs develop in water and produce a ciliated embryo or miracidium, which penetrates certain species of snail ; after a period of development in the snail the organisms enter the water as cercariæ, which may be either encysted or free-swimming. The cercariæ are either swallowed in drinking water or may burrow through the unbroken skin, and thus the life-cycle is completed.

Bilharziasis (*Schistosomiasis*).—Two common forms of the disease are encountered, one due to the *Bilharzia hæmatobia* and the other to *Bilharzia mansoni*. In both, the flukes inhabit the smaller veins, and produce eggs which are discharged into the bladder in the first type and through the wall of the colon in the second. The eggs are oval bodies of relatively large size (about 150 μ in length) ; in the case of the hæmatobia variety there is a sharp terminal spine, while the mansoni variety has a lateral spine. The symptoms in bilharziasis are due not to adult flukes in the blood but to local irritation in the bladder or rectum from the passage of ova through the walls of the viscus.

Bilharziasis is widely distributed, particularly in Egypt and South Africa. Infection arises from bathing in water containing the free-swimming cercariæ, which penetrate the intact skin. In some areas the disease is extremely common. A third species, *Bilharzia japonica*, occurs in the Far East and causes an intestinal bilharziasis characterised in its later stages by great enlargement of the spleen and liver.

Symptoms.—In the disease due to *Bilharzia hæmatobia* the main symptom is hæmaturia, due to irritation of the bladder. At the end of micturition a few drops of blood are passed and numerous ova are found in the urine. Sometimes the chronic bladder irritation may lead to abscesses and calculi, but often the hæmaturia persists for years without serious symptoms. With the *Bilharzia mansoni* infections, the lower part of the colon and the rectum are mainly affected. The mucous membrane becomes thickened and polypoid, the stools contain blood and mucus, and ova are discharged in the fæces. In some cases the liver may become cirrhotic and ascites develop. Eosinophilia is often present.

Treatment.—Intravenous injections of tartar emetic are most effective. The initial dose for an adult is $\frac{1}{2}$ gr. in 10 c.c. of sterile saline, and the injection

is repeated on alternate days, increasing the dose up to a maximum of 2 gr. A total amount of about 25 gr. should be given. Fouadin (Bayer) can be given intramuscularly. The initial dose is 1·5 c.c., on the second day 3·5 c.c., and subsequently 5 c.c. on alternate days until a total of 40 c.c. has been given. Anthiomaline (May and Baker) is also effective. Prophylaxis depends on avoiding bathing in infected water and the prevention of evacuation of urine or fæces near or into water.

DISEASES DUE TO TAPE-WORMS

Cestodes or tape-worms inhabit the upper portion of the alimentary canal in man and other animals, and discharge their ova in the fæces. The ova are ingested by a secondary host, and larval forms develop in its muscles and other viscera. When the secondary host is eaten by the original host the larvæ are ingested and develop into mature tape-worms.

In most cases of tape-worm infection in man, the adult worm lives in the intestine, but in one important group, the *Tænia echinococcus*, the primary host is the dog, and development of the larvæ occurs in the viscera of man and produces what is known as hydatid disease. The tape-worms which inhabit the human intestine are the following: (i) *Tænia solium*, (ii) *Tænia saginata*, (iii) *Dibothriocephalus latus*.

There is a great variation in the size and morphology of the different forms of tape-worm, but generally speaking their structure is similar, and consists of a head portion or scolex and a number of flattened segments which are posterior to the scolex. There is no alimentary canal, and the segments derive their nutrition by direct absorption of the intestinal contents. Each segment contains differentiated sexual organs, and when fully developed contains ripe ova. As the worm grows, segments are discharged in the fæces.

Tænia Solium.—This tape-worm is common in Northern Europe. Its secondary host is the pig, which becomes infected by eating ova discharged in human fæces. In the pig, the ova develop into small oval vesicles, the *Cysticercus cellulosæ*, which are found in the skeletal muscles and are about 20 mm. in length. If these are eaten by man the *Cysticercus* develops into an adult *Tænia solium* in the intestine. The *Cysticerci* are destroyed by cooking, and therefore the disease is only prevalent in countries where ham is eaten raw or partially cooked.

Tænia solium is 6 to 9 ft. in length, with a globular head armed with a double circle of hooklets and four suckers, by means of which it attaches itself to the mucous membrane of the intestine. The head is extremely minute as compared with the size of the ripe segments and does not exceed 2 to 3 mm. in diameter.

Symptoms.—Often there are no symptoms beyond the passing of segments of the worm in the fæces. Sometimes there is vague abdominal discomfort, with a voracious appetite. Usually there is no impairment of the general health, but the patient may become very neurotic. An eosinophilia is sometimes found, though anæmia is unusual.

Treatment.—The object of treatment in all types of intestinal tape-worm infection is to effect a complete evacuation of the worm, including the head portion. If the latter remain, it will produce further segments in the course

of a few months. The drug which has a specific anthelmintic effect on tape-worms is male fern. Details of treatment are as follows :—

The patient is put on a very light diet for two days before the male fern is to be administered, and the bowels are kept freely open with saline purgatives. Food is withheld entirely after midday on the second day of treatment. On the morning of the third day two doses of the following mixture are given at half an hour's interval: Ext. filicis liq. ʒi, Syrup. Zingiber ʒi, Gum acacia gr. xxx, Aqua ad ʒi.

The male fern is liable to produce nausea, which may to some extent be avoided by taking a cup of black coffee between the doses. After the last dose of male fern a strong saline purge is taken to effect the discharge of the worm. Careful search of the fæces should be made for the head of the worm : if this remains unpassed, segments may reappear in the stools in three months and a further treatment is required. Castor oil must be avoided when male fern is employed, as toxic effects may occur.

When treatment by male fern is unsuccessful, pelletierine tartrate, alkaloids derived from pomegranate, may be tried. This drug is given on an empty stomach in a capsule in doses of 2 to 4 gr., and is followed two hours later by a purgative.

Tænia Saginata.—This worm in the adult form is several yards long, and the head is equipped with suckers but no hooklets. The larval stage occurs in the cow, where it is known as the *Cysticercus bovis*. The cysts are found mainly in the muscles of mastication. The symptoms and treatment are similar to those described above.

Dibothriocephalus Latus.—This worm is very long and has an enormous number of broad segments. It is found chiefly around the Baltic, and the larval stage is passed in certain fish, the eating of which, insufficiently cooked, produces infection in man.

Infection with the *Dibothriocephalus* may produce a severe megalocytic anæmia. Possibly this is due to defective absorption of " anti-anæmic principle " (*vide* p. 267). Male fern is usually an effective anthelmintic.

Somatic Tæniasis (Cysticercosis).—The cysticercus cellulosæ stage of *Tænia solium* may occur in man. This results from ripe segments of the worm reaching the stomach during an attack of vomiting, or by accidental swallowing of the ova. In such cases the *Cysticerci* may develop in the muscles or brain, where they may produce epileptic fits.

Hydatid Disease

Whereas in the other forms of tape-worm the adult worm lives in man, in disease due to *Tænia echinococcus* the larval stage is passed in man, and the mature worm inhabits the intestines of animals, chiefly the dog. The disease, specially common in Australia, also occurs elsewhere. Human infection results from close contact with dogs, which discharge ova in their fæces. The worm itself is very minute, and does not exceed 5 mm. in length ; the head is provided with four suckers and a double row of hooklets ; there are only three segments, the last of which alone produces ova.

When the ovum is swallowed by man the embryo is liberated, and ultimately reaches the blood stream after burrowing through the wall of the intestine. It may be carried in the blood to the liver, the lungs, the kidneys, or the brain. Having eventually come to rest in one or other

viscus, most commonly the liver, the embryo is converted into a small cyst with two definite layers, an external laminated membrane and an internal parenchymatous layer, the endocyst. As a result of local tissue irritation a fibrous capsule is formed, shutting off the cyst from the surrounding tissues. As the cyst increases in size, buds develop from the inner parenchymatous layer and become daughter cysts, which again in turn produce granddaughter cysts. In this way the original cyst gradually enlarges, and may contain large numbers of smaller cysts. From the inner layer of the cysts further buds arise, which develop into brood capsules. These buds form scolices, which represent the head of the *Tœnia echinococcus* with its sucking discs and a circle of hooklets. The fluid in the cyst is clear and non-albuminous, with a specific gravity of about 1,005, and the characteristic hooklets may be found in the fluid.

The echinococcus cysts may remain alive for an almost indefinite period, but sometimes they die and the cyst becomes inspissated, and sometimes partly calcified. In other cases rupture takes place as the cyst enlarges, and the daughter cysts and scolices are discharged into the lung, peritoneum, pericardium, or to the exterior. Lastly, the cyst may become infected and suppurate.

Approximately 70 per cent. of hydatid cysts occur in the liver. The symptoms produced will depend entirely on the site of the cyst and on such accidental occurrences as its rupture or suppuration.

Hydatids of the Liver.—The liver may become very much enlarged as the result of the presence of hydatids. The physical signs will vary with the part of the organ which is involved. If the cyst is in the right lobe near the posterior surface, the liver is enlarged upwards towards the pleural cavity, and there is dullness on percussion over the right base and in the posterior axillary line. With great enlargement there is bulging of the right side of the thorax, especially in the lower portion. When the cyst occupies a position in the anterior part of the liver a swelling may be felt in the epigastric region, which has a tense, firm feeling and a smooth surface. When the cyst is superficial, a *hydatid thrill* may occasionally be elicited if the tumour is palpated with one hand and tapped gently with the fingers of the other hand. With cysts in the left lobe of the liver the heart is displaced upwards, and there is an increased area of dullness in the left hypochondrium.

Symptoms may be completely lacking, and there is seldom any general disturbance of health. With large tumours there may be sensations of dragging or pressure in the region of the liver.

With suppuration serious symptoms develop and the case resembles one of hepatic abscess, with rigors, pyrexia, sweating, and sometimes jaundice. If the cyst perforates into an adjacent viscus, its contents may be coughed up should the perforation be into the lung ; or in the cases of perforation into the alimentary tract, portions of the cyst may be vomited or passed in the fæces.

The diagnosis of hydatid cyst may be suspected when there is marked hepatic enlargement which has been observed to be present over a long period without impairment of health. The condition has to be differentiated from growths of the liver, syphilitic cirrhosis, tropical or other abscesses, and right-sided pleural effusions. Points in favour of hydatid are bulging of the chest wall, a smooth surface to the tumour, and the presence of the

hydatid thrill. Eosinophilia is common in patients with hydatid disease, and a blood count is always advisable with obscure hepatic enlargements. As a further aid to diagnosis a complement fixation test may be performed, but the results of the test cannot be regarded as conclusive. This is also true of the skin reaction test of Casoni, in which a few drops of hydatid fluid are injected intradermally. The immediate appearance of an urticarial wheal at the site of injection usually indicates that the patient harbours hydatids.

Hydatids of the Lung and Pleura.—The cysts compress the lung, and ultimately lead to hæmoptysis, inflammation, and gangrene.

Hydatids of the Kidneys.—This condition is rare. The kidney may be converted into an enormous cyst resembling a hydronephrosis. Small cysts and hooklets may be passed in the urine, with accompanying attacks of renal colic.

Hydatids of the Nervous System.—Symptoms of cerebral tumour are produced with headaches, convulsions, and sometimes insanity.

Treatment of Hydatids..—Unfortunately, no drug has any effect upon hydatids. Treatment is entirely surgical, and in the case of hydatids of the liver involves either complete removal or drainage of the cyst. Care must be taken to avoid dissemination of the cysts in the course of operation.

DISEASES DUE TO ROUND WORMS

There are a number of Nematodes or round worms which infect the human intestine. The most important of these are *Ascaris lumbricoides*, *Enterobius vermicularis*, *Trichuris trichiura*, *Ankylostoma*, and *Trichinella spiralis*. In addition to the intestinal nematodes, the *Filarioidea* inhabit the lymphatic vessels, and the guinea-worm the tissues of the foot. Unlike the tape-worms, round worms have an alimentary canal and are not composed of separate segments.

Ascaris Lumbricoides.—This worm is 6 to 10 in. in length and reddish-brown in colour. Ova are passed in the fæces. These are brown oval bodies about 70 μ in length and 60 μ in width. Autoinfection can take place by their transfer from the anus to the mouth.

Usually Ascaris is found in the small intestine, but sometimes the worms may enter the stomach and be vomited. More rarely they have been found blocking the common bile-duct or in the appendix. Often no symptoms are produced. Sometimes, however, the presence of round worms may lead to the passage of blood and mucus in the stools, which may be mistaken for dysentery ; more often flatus and distension are troublesome symptoms. Should a worm die and remain in the upper intestine, toxic absorption occurs, with pyrexia and vomiting. The worms are often passed in the stools, and a patient who knows himself to be infected is liable to develop various neuroses.

Treatment.—Santonin (2 to 5 gr.) is given on three successive nights followed by castor oil in the morning. Occasionally it produces vertigo and yellow vision.

Oxyuriasis.—The *Enterobius vermicularis*, often known as the *Oxyuris vermicularis*, is the thread-worm, which inhabits the colon and particularly the rectum. It is only about $\frac{1}{2}$ in. long. Ova and worms are found in the

fæces, and the main symptom produced is itching around the anus, particularly at night. The patient is usually a child, and the most satisfactory treatment is to wash out the rectum and lower bowel with an infusion of quassia (1 in 40): this procedure should be repeated every other day for a fortnight. Saline purgatives will help to dislodge the worms, and the itching is treated by application of ung. hydrarg. nit. dil. It is important to avoid autoinfection by washing the hands and perineum thoroughly after defæcation.

Trichuris Trichiura (*Trichocephalus dispar*).—This worm is commonly known as the whip-worm, and is about $1\frac{1}{2}$ in. in length. The hinder portion of the worm is very thick and the anterior thin and hair-like, a peculiarity which gives rise to its popular name. No symptoms are usually produced. All forms of treatment are ineffective.

Ankylostoma Duodenale.—Whereas all the round worms described above produce but few, if any, symptoms, the ankylostoma or hook-worm is a serious menace, if not to life, at any rate to health, and produces the disease known as ankylostomiasis. The parasite exists in almost all parts of the world, but particularly in the tropics. Epidemics have occurred among miners in Cornwall, Germany, and Switzerland.

Life History.—The adult worm is about 10 to 15 mm. in length, and the mouth is provided with two pairs of sharp hook-shaped teeth with which it pierces the mucous membrane of the intestine. The ova are passed in the fæces, and if they fall upon warm soil they develop into larvæ, which are able to penetrate the intact skin. After entering the veins they pass upwards through the heart into the pulmonary circulation, from which they burrow into the bronchi. They then ascend through the trachea, and after passing the larynx go down the œsophagus to develop into adult worms in the upper part of the small intestine.

Infection occurs in man if the feet are exposed to mud or water in which the embryo worms are present: this explains epidemics among workers in mines and tunnels. The disease can only occur where proper sanitation is lacking.

Ankylostomiasis.—The parasites produce a local lesion at their site of entry, which is most commonly on the feet or hands. Small vesicles and pustules are formed, with some local inflammation which subsides in the course of a few days. The local lesions are described as "ground-itch."

The general symptoms depend partly on the number of worms which infect the intestine, and partly on the reaction of the individual patient. In many regions as many as 90 per cent. of the population are infected, as judged by the finding of ova in the fæces, but only a proportion show symptoms.

The main clinical features are hypochromic anæmia, abdominal discomfort, failure of nutrition, and lassitude. In children growth is markedly stunted. The hæmoglobin may fall to 30 per cent. with marked œdema, and death may occur from exhaustion and intercurrent infections. Eosinophilia ranges from 10 to 30 per cent. Gastro-intestinal symptoms are sometimes present and perversions of appetite occur, as the result of which patients may eat earth, clay, hair, or paper. Severe anæmia causes dyspnœa and cardiac dilatation.

Diagnosis.—This can be made definitely by the discovery of ova in the fæces; these are oval bodies about 60 μ in length and 40 μ in breadth.

The ova have thin transparent capsules enclosing a number of cells. Eosinophilia with anæmia is highly suggestive of ankylostomiasis.

Prophylaxis and Treatment.—The Rockefeller Foundation has inaugurated a world-wide campaign against ankylostomiasis, which is already producing satisfactory results. In the prophylaxis of the disease sanitation is of the greatest importance, and with properly constructed latrines the incidence of the disease is greatly decreased. When the disease is prevalent the population must be educated to understand the dangers of indiscriminate defæcation, and also the necessity for treatment of infected individuals.

As an anthelmintic, tetrachlorethylene is safe and effective. Four cubic centimetres are given in a single dose shaken up in 8 drachms of Epsom salts. This is taken in the early morning, and the salts are repeated in three hours if the bowels are not opened. Thymol is also employed. In adults three cachets of 30 gr. each are given at two-hourly intervals, followed by a saline purge. Thymol is soluble in fats and alcohol, which must therefore be avoided during treatment. Two further treatments should be given at weekly intervals.

Trichinella Spiralis.—This is an extremely small worm which inhabits the small intestine. The disease known as trichiniasis is produced, not by the presence of adult worms in the intestine, but by the migration of their embryos into the muscles.

Life History.—The adult worm inhabits the intestine of the pig, and produces large numbers of embryos which penetrate the wall of the gut and enter the blood stream, by which route they ultimately reach the skeletal muscles. Lodged in these they develop into small cysts about $\frac{1}{2}$ mm. in length. Within the cyst lies the embryo worm in a spiral coil. No further development takes place unless the flesh of the infected animal is eaten by man or other animal. If this occurs the cyst wall is digested, and the trichinella embryo rapidly grows into an adult worm in the intestine. The worm produces large numbers of larvæ, which migrate to the striated muscles, where cysts are formed. The encysted trichina may remain alive for many years, but in course of time the cysts may calcify, and are also readily destroyed by heat.

Trichiniasis.—This results from eating infected pork which has been insufficiently cooked, and is relatively common in Germany. Careful inspection of meat before distribution and the avoidance of raw or partially cooked ham prevent the dissemination of the disease.

Symptoms.—Soon after eating infected meat there may be abdominal pain, vomiting, and diarrhœa, but very often these symptoms are slight. The more serious symptoms arise between the seventh and the tenth days after infection, when the embryos are passing from the intestine to the muscles. At this stage there is usually considerable fever, and the migration of the parasites into the muscles causes an acute myositis, with much tenderness and pain. The temperature may simulate that of typhoid fever. A secondary anæmia develops, and the leucocyte count is high with a great increase in the eosinophils. Œdema of the eyes is often a striking clinical feature. In protracted cases there is much emaciation.

Diagnosis.—This may be made definitely by the removal of a small portion of muscle, in which the trichina cysts can be seen, or by finding the larvæ in samples of the pork which the patient has eaten. Eosinophilia

occurring in a case of continued fever should also rouse suspicion. The disease has to be differentiated from typhoid fever and acute rheumatism. In the latter disease the pain is in the joints and not in the muscles, while in typhoid, leucopenia and the absence of muscular pain and tenderness will assist in the diagnosis.

Treatment.—No satisfactory treatment is available which will affect the encysted embryos, but the alimentary canal should be cleared of the adult worms by calomel, castor oil, and salines. When the muscular pain is severe it must be relieved by sedatives.

Filariasis.—Several different genera of the order of filarioidea have been described, and are widely distributed in the tropics. The adult worms are thread-like organisms approximately 2 in. long, which inhabit the lymphatic system. They produce embryo worms which are less than $\frac{1}{2}$ mm. in length and of the diameter of a blood corpuscle. In the case of *Wuchereria bancrofti* the embryos appear in the peripheral blood during the night or while the patient is sleeping. For the full cycle of development to occur an insect (*e.g.*, mosquito in the case of *W. bancrofti*) is necessary as a secondary host. The latter, on sucking blood from an infected person, withdraws with the blood a number of filaria embryos, which undergo stages of development in the body of the insect. Ultimately the larvæ reach the proboscis and thus infect human beings.

Infection with filaria produces various symptoms dependent on obstruction of the lymphatics by the adult worms. The parts of the body most commonly affected are the legs and the scrotum, where the blockage of the lymphatics produces the condition known as *elephantiasis*, in which there is marked thickening and brawny œdema of the parts involved. A remarkable symptom which sometimes occurs in filarial infections is chyluria ; from time to time the patient passes white opaque urine which resembles milk. This phenomenon is due to a rupture of lymphatic vessels into the urinary tract.

There is no effective treatment for filarial infection, but chyluria may be diminished by restricting the amount of fat in the diet. Where the elephantiasis is localised, as in the scrotum, surgical removal is indicated.

Guinea-worm.—This worm occurs in parts of Africa and in the East Indies. It is found subcutaneously in the neighbourhood of the feet, where it forms a palpable coiled mass under the skin. Eventually the head of the worm ulcerates through the skin, and living embryos are discharged to the exterior. These develop in water and are ingested by a small crustacean, the cyclops, in which they develop. If the cyclops be swallowed in drinking water the larvæ grow into a mature worm, which later burrows from the intestine into the leg.

The head of the worm may be seen in the base of the ulcer. After discharging its embryos it often leaves the body spontaneously. Natives who are affected with guinea-worm roll it around a small stick, and each day wind a little more out until the entire worm is withdrawn. Care must be taken not to rupture the worm, which is about 18 in. in length.

J. J. Conybeare.

DISEASES OF INFANTS

THE manifestations of disease in infancy are influenced by a number of factors which are peculiar to this age. Of these, immaturity of every system, extremely rapid growth, peculiarities of immunity, and the transition from intrauterine life to the outside world are the most important. It follows that certain conditions will only be observed in infancy, others (such as rickets) will have their maximum incidence closely related to a particular phase of growth, whilst others which are common to infancy and adult life may show characteristic manifestations when they occur during the earliest weeks or years.

At birth the infant is already the product of his heredity and environment; the comparatively recent recognition of the significance of the rhesus factor, maternal infection and maternal diet as possible causes of fœtal abnormality have focused attention on the antenatal aspects of pædiatrics, whilst at the same time the possible influence of environmental factors on genes during development has led to a more realistic conception of "nature" and "nurture" often acting together in the determination of disease processes or abnormalities.

In Great Britain the present century has seen a profound fall in the infant mortality rate (deaths under one year per thousand live births); but if this mortality is subdivided into neonatal mortality (deaths under one month) and deaths between one month and one year, it is found that the improvement is seen principally amongst the older infants. The newborn period, which is arbitrarily regarded as being the first month of life, therefore deserves particular attention if the infant mortality rate is to be still further reduced.

DISEASES OF THE NEWBORN

Prematurity

Since prematurity is directly or indirectly responsible for more than 50 per cent. of neonatal deaths, it must be regarded as a condition of prime importance in infancy. For statistical purposes an infant is regarded as premature if it weighs $5\frac{1}{2}$ lbs. (2,500 gm.) or less at birth. Whilst in practice there is not such a simple relationship between birth weight and maturity, it is in general true that infants weighing less than $5\frac{1}{2}$ lbs. will require special care, and that the prospects of survival diminish with diminishing birth weight. When the infant weighs less than $2\frac{3}{4}$ lbs. (1,250 gm.) at birth, or the period of gestation is less than twenty-eight weeks, survival is rare even under optimum conditions.

The causes and prevention of prematurity lie within the field of obstetrics and antenatal care; inadequate maternal diet during pregnancy, toxæmia, and infection are all important causes, though maternal syphilis (at one time responsible for a large number of premature or still-births) is becoming

relatively less significant with improved antenatal supervision and routine Wassermann examinations during the earlier months of pregnancy.

The premature is even less able than the full-term infant to withstand trauma or infection, whilst the adjustment to extrauterine life is made with greater difficulty. Thus even the easy transit through the birth passages, which is to be expected in the case of a small infant, is liable to cause intracranial injury owing to the immaturity of the tissues; the establishment of respiration is often precarious, and followed by partial atelectasis and more or less prolonged periods of apnœa or cyanosis; the infant readily succumbs if chilled; and owing to the immaturity of the gastro-intestinal system, digestion is so readily overtaxed that feeding requires the greatest care and patience. It is often found that physiological jaundice (*vide* p. 174) is more marked and more prolonged in the premature than in the full-term infant, whilst some degree of anæmia during the first two months of life is almost invariable. Unless protected early, the premature is peculiarly liable to develop rickets and to a less extent infantile scurvy.

The appearance of the premature infant at birth, small size apart, is often characteristic. Relative lack of subcutaneous fat gives a wrinkled appearance to the skin, which may be covered with fine lanugo. The head is relatively large, and may later, owing to the rapid growth of the brain and separation of the sutures, give a false impression of hydrocephalus. In the smaller infants, movements and cry are likely to be feeble, respiration irregular, and temperature unstable.

Treatment.—Regulation of the temperature of the room or cot in which the infant is nursed is essential; infants weighing less than 4½ lbs. are best kept at a steady temperature of approximately 85° F., whilst for larger infants the temperature should be 75° F. The humidity should be high (approximately 65 per cent.) for infants under 4½ lbs. Whilst many maternity units have thermostatically controlled premature nurseries, almost equally good results can be obtained in the home with all except the smallest prematures if attention is paid to cot-warming and nursing. In the case of the smaller prematures, however, and those in whom there is any tendency to cyanosis, the use of oxygen is likely to be necessary.

Handling should be gentle and reduced to a minimum, though where there has been inhalation of liquor amnii frequent changes of position to promote drainage should be made. The premature infant should not be bathed, but the skin cleaned with olive or cod-liver oil. Attendants should wear masks and visitors should be excluded.

The technique of feeding will depend on whether the infant can suck and swallow, or swallow but not suck, or is unable even to swallow without danger of exhaustion or inhalation of milk. In the first instance a bottle fitted with a small teat can be used; in the second, milk can be given by pipette; and in the third case all feeds must be given by tube. In general, overfeeding during the first days or weeks is a greater danger than underfeeding, and it is usually satisfactory if the infant maintains its weight for the first two to three weeks; with increasing maturity of digestion, a steady weight-gain can then be expected. Nothing need be given by mouth during the first twelve hours, after which 1 to 2 drachms of 5 per cent. glucose is given three-hourly for twelve hours. Subsequently diluted breast-milk followed by whole breast-milk should be given, or if this is unobtainable, a formula of half-cream dried or evaporated milk with added sugar.

Jaundice during the Neonatal Period

Physiological Jaundice (Icterus Neonatorum) occurs in all infants during the first week of life, though it is not always clinically recognisable. It is due to a combination of two processes—destruction of fœtal hæmoglobin and a partial inability of the immature liver to excrete bilirubin. The jaundice may persist for a variable time, but seldom for more than two to three weeks. It is not clinically significant, except that the presence of jaundice is a contraindication to operation. The liver and spleen are not enlarged, and the stools and urine are normal.

Congenital Obliteration of the Bile-ducts gives rise to a more intense jaundice, which may vary in degree but shows a general tendency to increase over a period of weeks or months. It is essentially obstructive in type, and is associated with pale or clay-coloured stools and bile-stained urine. The spleen may be enlarged, and there is progressive cirrhosis of the liver. The symptoms vary considerably in severity, and the condition is compatible with comparatively good general health for as long as a year or more. In other cases vomiting and failure to gain weight are noticed early. The congenital malformation varies from complete obliteration of the bile-duct system to a localised deformity of the common bile-duct. Since the condition is fatal if untreated, surgical exploration is indicated, though the percentage of cases in which surgical reconstruction is possible is very small.

Icterus Gravis Neonatorum is one manifestation of congenital hæmolytic anæmia or erythroblastosis fœtalis. The condition arises from the mating of a father whose blood contains the rhesus antigen with a rhesus-negative mother. When a rhesus-negative mother conceives a rhesus-positive fœtus, there is a danger of fœtal blood cells entering the maternal circulation, and, acting as an antigen, stimulating the production of maternal antibodies. This sensitisation of the mother takes place relatively slowly, and in the case of the first pregnancy is often insufficient to affect the child. When, however, there is a high degree of antibody formation, the red cells of the fœtus or newborn infant are hæmolysed. The extent to which jaundice or anæmia dominates the clinical picture will depend to some extent on the stage at which the antigen-antibody reaction occurs, but it should be realised that the ætiological factors in the production of hydrops fœtalis, hæmolytic anæmia of the newborn, and icterus gravis are essentially the same. Previous transfusions or intramuscular injections of rhesus-positive blood to a rhesus-negative mother will tend to increase the severity of the reaction, whilst increasing sensitisation by successive rhesus-positive pregnancies will often give a characteristic history of a first child being unaffected, a second infant showing severe jaundice, and later pregnancies resulting in still-births.

The condition should be regarded as essentially a generalised antigen-antibody reaction, in which not only the infant's red cells but also the blood-forming organs are affected. In the deeply jaundiced cases, more or less extensive destruction of the liver occurs, and in those cases which survive there is likely to be some degree of hepatic cirrhosis.

The infant is frequently jaundiced at birth, and there may be yellow staining of the vernix caseosa. The jaundice rapidly deepens, and is associated with lethargy, vomiting, and progressive anæmia. Some œdema is commonly present. The spleen is enlarged, and the blood commonly shows well-marked erythroblastosis. Although the jaundice is primarily hæmolytic

in origin, there will be bile in the urine and the stools may be paler than normal. A complication which is seen in a small proportion of cases is kernikterus (bile staining and degeneration of the basal ganglia), which in infants who survive is likely to give rise to athetosis or mental defect.

Treatment consists of blood transfusion from a rhesus-negative donor who has not been sensitised to rhesus-positive cells. This will serve to replace the hæmolysed red cells, but unless exsanguination transfusion is practised, will not get rid of the circulating maternal antibodies. It is usually necessary to give an initial large transfusion and repeat as required, depending on the progress of the anæmia. In spite of any form of treatment, there is a mortality of 10 to 20 per cent., post-mortem examination in these cases usually showing extensive liver damage.

Jaundice due to Sepsis may occur from infection of any organ, but is most likely to result from umbilical sepsis which has ascended via the umbilical veins and reached the liver. The infant should receive intensive penicillin treatment, and if a septic clot is present in the umbilical veins, these should be ligatured and the clot evacuated. The prognosis is bad if the infection has reached the liver.

Congenital Syphilis should be kept in mind as a possible cause of jaundice during the newborn period, and other signs of the infection looked for (*e.g.*, enlarged liver and spleen, rhagades, snuffles, peeling of palms and soles, skin rashes, or condylomata). In any doubtful case where it is impossible to get the mother's Wassermann reaction and where the infant may give a false negative result, the long bones should be X-rayed. The moth-eaten appearance at the ends of the long bones, especially when associated with periostitis, is often diagnostic.

Birth Injury

Some degree of trauma during even normal labour is inevitable, and otherwise normal newborn infants may show red cells in the cerebrospinal fluid. Moulding of the skull is not in itself significant, though where there is extensive overriding of cranial bones there is a danger of laceration of intracranial vessels.

Cephalhæmatoma is of relatively common occurrence, and consists of subperiosteal hæmorrhage, which may result in a swelling (usually in the parietal region) reaching the size of half an orange. If there is no bony or intracranial injury associated with it, the condition is not clinically important, and though unsightly the swelling ultimately calcifies and finally becomes unnoticeable. It should not be aspirated.

Intracranial Injury varies from minor degrees of hæmorrhage or concussion to major tears of the falx or tentorium. The infant is likely to appear flaccid at birth, and respiration is established and maintained with difficulty. Other cases show restlessness, twitching, high-pitched cry, and some general spasticity. Where there is extensive hæmorrhage, the anterior fontanelle may be tense or bulging. Sedatives (chloral hydrate or chloral and bromide) should be given where there is restlessness or twitching, and continuous oxygen employed where there is cyanosis or respiratory embarrassment. Since these cases often show associated atelectasis, 5 per cent. CO_2 in oxygen may be given for short periods at hourly intervals. The infant must be treated for shock, attention being paid to the maintenance of temperature, and handling reduced to a minimum.

Fortunately many infants who show cerebral signs during the newborn period recover completely; others are left with residual hydrocephalus, mental defect, or cerebral palsy. Extensive lacerations and gross intracranial hæmorrhage are likely to prove fatal.

Palsies due to traction on the brachial plexus are described on page 709.

Hæmorrhagic Disease of the Newborn

Whilst hæmorrhage during the neonatal period may be due to trauma or secondary to jaundice or infection, a type of hæmorrhage is seen during the first two to five days of life which is closely related to the physiological fall in prothrombin which normally occurs after birth. When this fall becomes exaggerated, spontaneous hæmorrhage occurs from the umbilical cord, gut, or genito-urinary tract. Melæna is a common presenting symptom, and the loss of blood may be considerable before the condition is recognised. Either the bleeding or clotting times of the blood may be increased, though the findings are not constant. The prothrombin level, however, is consistently reduced.

Treatment consists in the immediate administration of vitamin K, accompanied if necessary by transfusion. Whilst vitamin K will raise the prothrombin level and cure the condition in twenty-four to forty-eight hours, the newborn infant is not well able to withstand loss of blood, and if the hæmorrhage has been considerable, transfusion should not be delayed. Administration of vitamin K in 5 mg. daily doses should be continued for three to five days.

Pneumonia and Atelectasis in the Newborn Period

Pneumonia in the newborn requires special consideration, as the clinical picture often differs profoundly from that of pneumonia in later life, and the condition is frequently found at post-mortem when its presence has not been previously suspected. It is particularly liable to occur in premature and feeble infants, and the inhalation of liquor amnii or vomitus is a predisposing cause. It is frequently associated with atelectasis, and even on histological examination it may sometimes be difficult to distinguish the primary condition.

The temperature is often normal or subnormal, and the respiration may be rapid, irregular, or characterised by periods of apnœa and cyanosis. The infant appears collapsed and fails to suck or gain weight normally. It is often impossible to elicit signs of consolidation, though moist râles at the bases or throughout the lungs are a frequent finding. In some instances diarrhœa or vomiting is the presenting symptom.

Treatment.—Care must be taken to see that the respiratory passages are clear after birth, and if liquor has been inhaled it should be sucked out of the nasopharynx, and the infant so placed that fluid can drain from the lungs. Subsequently, frequent changes of position to promote drainage are necessary. When pneumonia is suspected, the infant should be given full dosages of penicillin and nursed in an oxygen tent.

Atelectasis, like pneumonia, is also liable to occur in feeble and premature infants, and also in those who have suffered cerebral birth injury. It is probable that even in the normal infant full expansion of the lungs is only attained gradually after birth. When the infant fails to cry lustily and

respiration is feeble or the respiratory passages obstructed, atelectasis persists to an abnormal degree. The colour remains dusky, and on auscultation the breath sounds appear feeble. Respiration may have a grunting character.

Treatment is similar to that of pneumonia, but in addition 5 per cent. CO_2 in oxygen should be given for five minutes every hour, or whenever respiration becomes particularly feeble.

ANÆMIA IN INFANCY AND CHILDHOOD

Congenital Hæmolytic Anæmia (*Erythroblastosis Fœtalis*) has been referred to under Icterus Gravis Neonatorum, and is a manifestation of the same disease. Whilst some degree of jaundice is likely to be present, the anæmia may be the more striking sign. The diagnosis is confirmed by the enlargement of the spleen, the presence of large numbers of erythroblasts and nucleated red cells in the peripheral circulation, the family history, and finally by the rhesus constitution of parents and infant, and by the presence of high antibody-titre in the mother's blood. The infant's blood gives a positive Coomb's test. The treatment is the same as for icterus gravis neonatorum. The prognosis appears to be somewhat better in the absence of severe jaundice, as the liver is likely to be less extensively damaged.

Iron-deficiency Anæmia is the commonest form of anæmia in infancy, and is present in slight degree in a considerable proportion of artificially fed infants reared in poor urban conditions. When infants are kept on an exclusively milk, or milk and carbohydrate, diet into the second year, the hæmoglobin may fall to 40 per cent. or less and the anæmia be associated with œdema of the face and ankles and with splenomegaly. In premature infants, who are born with a deficient store of iron in the liver, anæmia develops relatively early (during the first three months of life) and cannot be completely prevented by the administration of iron. In full-term infants on an iron-deficiency diet, anæmia is more likely to be seen from six months to two years of age. The anæmia is microcytic in type, and in the absence of infection responds readily to the administration of iron and correction of diet. In some cases it has been found that iron containing traces of copper has proved more effective than purified iron preparations.

Cooley's Anæmia (*Mediterranean Anæmia*) is confined to children of Mediterranean stock, and is thought to be congenital in origin. The anæmia is chronic and progressive, and is associated with splenic enlargement; the liver may be enlarged also. The peripheral blood shows irregular, fragmented and nucleated red cells, which are hypochromic. Affected children develop a characteristic mongoloid facies and greenish pallor, whilst the bones, particularly of the skull, show a peculiar trabeculation due to hyperplasia of the bone marrow. No treatment is yet known to be effective.

Infective and Toxic Anæmia.—Anæmia occurs readily in infancy as the result of infection and the action of various toxins. These conditions may produce hæmolysis or suppression of blood formation. Deficiencies other than iron (*e.g.*, vitamin C and thyroid) may result in anæmia which will only respond when the primary deficiency is made good. Cœliac disease is also commonly associated with anæmia, but as this may be either microcytic

or macrocytic in type its ætiological relationship to the steatorrhœa is not clear. In general, the treatment of such anæmias is that of the primary cause, though where a severe degree of anæmia has developed, recovery may be hastened by blood transfusion.

Von Jaksch's Syndrome (*Pseudoleukæmia Infantum*).—This syndrome, which consists of anæmia and splenomegaly associated with a high leucocytosis (30 to 50,000 W.B.C.), is sometimes observed in infants in the second or third year of life. It is not a disease entity, and modern hæmatological methods usually make it possible to classify the cases according to the type of anæmia present or the primary cause.

GASTRO-INTESTINAL DISORDERS IN INFANCY

Under this heading are included a group of disorders characterised by diarrhœa and vomiting and responsible for a high infant mortality. Whilst the true dysenteries can be separated on clinical and bacteriological grounds, there remains a variety of cases in which different ætiological factors operate, but which show a similar clinical picture and comparable epidemiological behaviour. Of the various descriptive names that have been applied, *e.g.*, Summer Diarrhœa, Cholera Infantum, Gastroenteritis, the least controversial is probably Alimentary Toxicosis. This title is preferred, since it does not imply that the condition is one exclusively of the summer months, or that it bears any relationship to cholera asiatica, or that inflammation of the stomach and intestines is consistently present.

Ætiologically, the group may be classified into (i) those cases showing evidence of infection, either enteral (dysenteries, typhoid, paratyphoid) or parenteral; (ii) those where environmental factors appear primarily responsible; (iii) those in which food has precipitated gastro-intestinal upset; and (iv) those of unknown ætiology. Both those where there is a known infection present, and those where other factors appear primarily responsible, are, however, themselves infectious; this is most clearly seen where large numbers of infants are grouped together, and where the introduction of a single case of alimentary toxicosis may initiate an epidemic. It has been suggested that a virus infection, acting with or without other precipitating factors, might best explain the epidemiology of the condition, but conclusive proof of this theory is so far lacking.

Bacterial Dysentery.—The commonest type of bacterial dysentery observed in infants in Great Britain is that due to *B. sonne*, and this infection may assume epidemic proportions in institutions. It is particularly difficult to eradicate, owing to many patients remaining carriers after clinical recovery, and the frequent occurrence of subclinical and mild cases amongst older children. The infection is usually mild except in the younger age-groups, when it may prove fatal. The great majority of cases show blood in the stools at the onset (sometimes in a single stool) and subsequently the presence of mucus.

Typhoid-paratyphoid Group.—Typhoid only accounts for a very small proportion of cases of gastro-intestinal disorder in infants, but it is not uncommon for a paratyphoid organism (usually an atypical paratyphoid B.) to be identified in localised outbreaks. The clinical picture in such cases does not differ materially from that described below.

Parenteral Infection.—In addition to infections gaining entry via the gut (through the agency of contaminated milk or food), infection of organs other than the gut may result in diarrhœa and vomiting. This is particularly true of upper respiratory infections (including otitis media); the role of mastoiditis as a cause of diarrhœa and vomiting is more controversial, and though evidence of mastoid infection has been found in a high proportion of cases in certain epidemics, it is no longer considered justifiable to perform mastoidectomy without good evidence of infection being present. Every infant suffering from diarrhœa and vomiting, however, should be carefully examined for evidence of parenteral infection and sulphonamide or other appropriate therapy instituted if it is found.

Food.—Faulty feeding may precipitate diarrhœa and vomiting in one of three ways: a single indiscretion may serve as a gastro-intestinal irritant and provoke an acute attack; prolonged faulty feeding may lower the infant's resistance to infection; or contamination of milk may cause gastro-intestinal infection, or the products of bacterial action contained in it act as toxins. It is well recognised that in spite of the improvement that has occurred during the past century in the standard of artificial feeding, breast-fed infants are still considerably less liable to gastro-intestinal disorders than are the artificially fed. The commonest fault in artificial feeding is the prolonged use of foods, such as sweetened evaporated milk, which contain too high a percentage of carbohydrate. If in addition the infant's diet is deficient in vitamin D (see below), the fat and flabby product of this regime is peculiarly liable to diarrhœal upsets.

The best protection for the infant is breast-feeding during the first six months of life. If artificial feeding is necessary, the feeds should be prepared with scrupulous cleanliness and sterilised; when liquid cow's milk is used, added carbohydrate should represent not more than one-third of the total calories of the feed. The infant should receive a supplement of vitamin D daily from the age of three months.

Environmental Factors.—Infantile diarrhœa was previously a condition seen in epidemic form in the summer months, and considerable importance was attached in the ætiology to the occurrence of a high temperature (particularly of a high ground temperature) coupled with high humidity, in addition to contamination of food by flies. There can be little doubt that these factors may play a certain part in its ætiology, but since the incidence of the condition, which has shown a substantial general decrease in Great Britain in recent years, is often high in winter and early spring, it appears that temperature is not as all-important as was previously supposed. Overcrowding and bad hygienic conditions generally are undoubtedly important precipitating factors, and it is significant that in Greater London in the years 1930-38 the relative infant mortality from diarrhœa and enteritis was three times as high amongst illegitimate as amongst legitimate infants.

Epidemic Diarrhœa of the Newborn.—This condition may be considered separately from diarrhœa in older infants, since there is more experimental evidence that it is a virus infection and its occurrence in maternity hospitals amongst a particularly vulnerable age-group gives it a special importance. Numerous epidemics have been described recently throughout the northern temperate zone; the infectivity has been uniformly high, though the mortality rate has varied very considerably. In general the mortality rate

has been high, viz., over 40 per cent. In some epidemics, adults have been affected as well as infants ; in others, adults have apparently been immune. Unlike diarrhœa in older infants, breast-fed and artificially fed infants are equally affected. The incubation period is thought to be two to three days. The infant may fail to suck or gain weight during this period, or the first evidence of the disease may be the passage of an explosive watery stool. It is exceptional for the stools to contain mucus. The sudden onset and high infectivity makes early and satisfactory isolation extremely difficult, and it is usually necessary to close the unit in order to control the epidemic. Penicillin and sulphonamide treatment have usually been found ineffective, and therapy has generally to be confined to isolation and the general measures to combat shock and dehydration described below.

Clinical Picture of Diarrhœa in Infancy.—Since cases vary in severity from those where the condition is limited to the passage of loose stools without vomiting, to those in which the onset is fulminating, diarrhœa semi-continuous, and not even fluids can be retained by mouth, description will be confined to the moderately severe case. The picture is coloured by four processes : dehydration, due to excessive loss of fluid from the bowel and to a lesser extent from the stomach ; partial or complete suppression of urine ; acidosis (due to loss of sodium in the stools) and disturbance of potassium balance ; shock.

Dehydration is often of rapid onset and associated with equally rapid loss of weight. The skin becomes inelastic, the eyes sunken, and the fontanelle depressed. At the same time the urine becomes scanty and of high specific gravity, or secretion is altogether suppressed. The infant appears pale and toxic. Acidosis may be shown by lassitude and air-hunger. Though at first fretful and restless, the infant passes into a condition of more or less severe shock, in which it lies motionless and collapsed. The temperature may be raised or subnormal, high pyrexia usually indicating the presence of parenteral infection.

Treatment.—Shock must be treated by warmth and a minimum of handling, and dehydration by the administration of fluids. When the infant is cyanosed, continuous oxygen must be administered. If fluids can be retained by mouth, the stomach should be washed out with physiological saline, leaving 1 to 4 oz. in the stomach. The infant should then be given drachm doses of equal parts of physiological saline and 5 per cent. glucose, doubling the dose each half-hour until an ounce has been given. The interval should then be extended to an hour, and subsequently two hours. If vomiting is severe, all fluids by mouth should be omitted until they can be retained, and a continuous intravenous drip transfusion set up. The fluid used should be equal parts of 5 per cent. glucose (to combat ketosis) and physiological saline, until urinary excretion is re-established. Darrow's solution (containing KCl 2 gm., NaCl 3 gm., molar sodium lactate 40 c.c., water 710 c.c.) should then be given to correct the loss of intracellular potassium, alternated with 5 per cent. glucose. The danger of heart-block appears very slight if the giving of intravenous potassium is carefully controlled. After the initial dehydration has been corrected, blood or plasma diluted with an equal volume of physiological saline may be given to make good the depletion of plasma proteins which commonly occurs. Physiological saline (not glucose) may also be given subcutaneously in the early stages, but this has no advantage over the intravenous route and is apt to increase shock.

Injections of intraperitoneal saline are not recommended, as they increase the risk of basal pulmonary collapse and pneumonia.

Drugs play a relatively unimportant part in treatment. Succinylsulphathiazole (0·25 gm. per lb. body weight per day) will sometimes prove effective, but many cases fail to respond. Parenteral infection must be appropriately treated and, in more chronic cases, kaolin, bismuth, or charcoal may be tried. Stimulants may be used when there is circulatory failure, but the time-honoured use of brandy, unless this is well diluted, is probably liable to increase gastric irritability. In chronic cases care must be taken to cover the vitamin requirements.

The severe case of diarrhœa and vomiting is always likely to require hospitalisation, and full investigation should include estimation of CO_2 combining power of the blood, blood potassium level during therapy, and estimation of plasma protein.

HYPERTROPHIC PYLORIC STENOSIS

Ætiology.—The condition is almost certainly due to a recessive gene, though its occurrence is not explicable on simple Mendelian lines. Thus it is approximately five times as frequent in male as in female infants, and a disproportionately high percentage of cases are first-borns.

Clinical Features.—A careful history or observation will usually show that there has been slight, non-projectile vomiting in a previously healthy baby over a period of twenty-four or more hours, preceding the classical symptoms. This vomiting commonly appears in the second or third week, and very seldom earlier. It rapidly assumes a projectile character; the stomach-contents are forcibly expelled, usually during the latter part of the feed or within a few minutes of its completion. It is characteristic at first (before secondary gastritis has occurred) that the infant is not nauseated, and will feed again immediately after vomiting. Examination of the abdomen during the feed will show the presence of gastric peristalsis, passing from the left hypochondrium to a point immediately above and to the right of the umbilicus. The appearance has been compared to that of a golf-ball being rolled along beneath the abdominal wall. The peristalsis reaches a maximum immediately before the infant vomits, after which it ceases. Palpation of the abdomen will often reveal the presence of a small hard tumour, approximately in the position in which the peristalsis ceases. Though this is a valuable confirmatory sign, which will be elicited with practice in the majority of cases, failure to feel a tumour should not negative the diagnosis.

Unless the condition has been diagnosed early, it is only too common to find the infant has been taken off the breast, or the feed frequently changed, before the baby comes under observation, and in such cases the infant is likely to show severe wasting. Although constipation is the general rule, it should be remembered that an infant with pyloric stenosis of long standing may have developed a secondary diarrhœa, and presents a case of alimentary toxicosis.

The loss of fluid and chloride ions in the vomitus will tend to produce not only dehydration but some degree of alkalosis, though it is rare to see frank tetany unless this has been precipitated by the administration of sodium bicarbonate.

Diagnosis.—It is usually possible to make the diagnosis on clinical examination and history alone, but in doubtful cases the passage of a stomach tube and estimation of gastric residue, or X-ray examination, may provide confirmatory evidence. Mild cases, in which constipation is less marked, the vomiting less intractable, and no tumour is felt, are sometimes described as pylorospasm ; these respond well to medical treatment.

Morbid Anatomy.—The whole of the pylorus is thickened and hard, due to hypertrophy of the circular muscle fibres. In long-standing cases the stomach is dilated and the wall hypertrophied, whilst mucous gastritis is likely to be present.

Treatment.—Either medical or surgical treatment may be adopted, the choice depending on a number of factors which must be considered in each individual case. If the case is seen relatively early, vomiting is severe, and the infant in reasonably good general condition, surgical treatment is likely to give excellent results and the infant should have recovered safely within ten days. The Fredet-Rammstedt operation is that of choice ; the circular muscle fibres are divided throughout the length of the pylorus to relieve the obstruction, the operation being carried out under general or local anæsthesia. Pre-operative preparation is important, the stomach being washed out with physiological saline, and, if necessary, dehydration being corrected by an intravenous drip. The infant can be given 1 drachm of equal parts physiological saline and 5 per cent. glucose three hours after the operation, and the same dose repeated half-hourly for two hours. Expressed breast-milk or half strength half-cream dried milk can then be substituted at alternate feeds, the amount and interval being doubled at each feed until the infant is taking 1 oz. of milk feed. By the third day a breast-fed infant can be put back to the breast. Medical treatment may be adopted when the case is mild, *i.e.*, when a relatively small proportion of the food is being vomited and gastric residue is not great, when the patient is first seen after the tenth week, or when skilled surgical aid is not available. Some go so far as to attempt medical treatment in the first instance in all cases ; but it must be remembered that if medical treatment fails to relieve vomiting, the infant's general condition may deteriorate rapidly and the operative risk, if surgery has finally to be resorted to, becomes correspondingly increased. When medical treatment is adopted, eumydrin (atropine methyl nitrate) should be given twenty minutes before each feed, in doses of 1 to 3 drops of a 0·6 per cent. alcoholic solution placed on the infant's tongue ; or the same dosage (0·1 to 0·3 mg.) may be used in a lamella placed under the tongue. If the infant is artificially fed, the feeds should be thickened in the proportion of 1 in 20 with a cereal preparation.

In both surgical and medical treatment success will depend on treatment being given in time and on the prevention of cross-infection. If possible, the infant should be isolated and breast-feeding maintained or re-established. Where there is evidence of alkalosis or dehydration, physiological saline solution should be given parenterally and blood transfusion is indicated when anæmia is pronounced.

When more than a quarter of the birth weight has been lost, the results of surgical treatment are poor and those of medical treatment are worse. Otherwise a reasonably good prognosis can be given, provided that the infant is protected from cross-infection.

INFANTILE SCURVY

(*Barlow's Disease*)

Ætiology.—Infantile scurvy, like rickets, is a deficiency disease which is most likely to occur between the ages of six and eighteen months, when a solely milk diet is no longer sufficient for the growing infant's needs. Since the deficiency in the case of scurvy is a lack of vitamin C, the disease is most commonly seen in artificially fed infants where such vitamin C as the milk contains has been largely destroyed in preparation. Scurvy can occur, however, in breast-fed infants if the mother's diet is grossly deficient. There is commonly a time-lag of several months before the clinical manifestations of scurvy appear.

Morbid Anatomy.—Lack of vitamin C produces permeability of the capillaries, and consequently hæmorrhage. It also affects bone-formation. At the growing ends of the long bones, it is found that there is continued calcification of cartilage taking place, but the osteoblastic function is arrested. Thus there is a piling-up of calcified matrix, which can readily be recognised radiologically, and at the same time rarefaction of the metaphysis (the so-called Trummerfeldt zone) immediately beyond. Since the calcified matrix is brittle it commonly shows fragmentation, whilst the area of rarefaction may be so extensive that fracture occurs through it, with displacement of the epiphysis. The rarefaction of bone is not confined to the ends of long bones, and in advanced cases the whole of the long bones and epiphyses may show a ground-glass appearance on X-ray.

Since the disease is one affecting the whole capillary bed, hæmorrhage may occur in any site. Most characteristically it is seen beneath the periosteum of the long bones of the legs, and into the gums around erupting teeth. But in fatal cases it may be found in any organ. The bone marrow is commonly yellow in appearance rather than red.

Clinical Features.—Whilst some cases may give a history of ill-health, loss of weight, or pallor preceding the onset of acute symptoms, it is common for the disease to present suddenly in a baby who has previously been thought to be well. The first symptom complained of is frequently pain, the infant screaming if the legs are touched or moved. The thighs are held semi-flexed and abducted, in the "frog position," and the legs or knees may appear considerably swollen. Pseudo-paralysis may be observed, particularly if displacement of the epiphysis has occurred. Examination of the gums is likely to show hæmorrhage around the teeth, or the whole alveolar margin may be swollen and purple in colour. When the condition has not been recognised and the gums lanced, they may become necrotic and the teeth shed. Skin hæmorrhages or spontaneous bruising are of less frequent occurrence, but red cells in the urine are almost constantly present. Hæmorrhage into or around the orbit will cause exophthalmos or ecchymosis.

A most useful diagnostic sign is the presence of scurvy-beading of the costo-chondral junctions. Expansion of the end of the rib causes an enlargement on the rib side of the junction only, and a sharp ridge demarcating it from the costal cartilage can be felt. If, as sometimes happens, scurvy occurs in association with rickets, this ridge is less likely to be palpable.

Diagnosis.—If the typical clinical picture of scurvy is present, and red cells are found in the urine, the diagnosis should be clear. Confirmation

can be obtained from the dietetic history, radiological examination of the long bones, and, if necessary, estimation of vitamin C in the urine before and after a loading dose of vitamin C has been given. In the acute phase the most helpful radiological changes will be seen at the wrists or knees, the presence of excess of calcified matrix coupled with adjacent rarefaction being characteristic. It is unlikely that subperiosteal hæmorrhage will be demonstrated radiologically at this stage, but later, when it begins to calcify, it can be clearly seen.

In differential diagnosis acute rheumatism should cause no confusion, as infantile scurvy occurs under the age of two and rheumatism after that age. Osteomyelitis will be distinguished by the higher temperature (though this may be raised in acute scurvy), the white blood count, and the radiological appearance. Acute leukæmia may simulate scurvy closely, but by the time hæmorrhages are occurring there is likely to be more marked anæmia, whilst examination of the peripheral blood or of the marrow should make the distinction clear. Pseudo-paralysis may suggest the possibility of anterior poliomyelitis, but here the other signs of scurvy will not be present, whilst the onset of paralysis in anterior poliomyelitis is characteristically associated with stiffness of the neck and back.

Treatment and Prevention.—Since the cause of scurvy lies in a deficiency of vitamin C, prevention and cure lie in the administration of this vitamin in palatable form. It should be given as a routine to infants over the age of three months, this being particularly important in the case of artificially fed infants and prematures. The most satisfactory vehicle is orange juice, which is well tolerated by most infants. The orange juice must be freshly squeezed or specially prepared, and must not be heated, alkalinised, or allowed to stand in contact with the air, since its potency will be destroyed by so doing.

Other preparations which are rich in vitamin C are tomato juice, black currant purée, and elixir of rose hips, all of which have been extensively used when orange juice was not available or was not well tolerated. There is no advantage in giving synthetic ascorbic acid except for experimental purposes. For prevention, two teaspoonfuls of orange juice three times a day will cover the normal infant's requirements. In treatment, 1 to 2 oz. of orange or tomato juice three times a day, or 100 to 300 mg. of ascorbic acid daily should be given by mouth, and will usually relieve symptoms within a week. If the infant fails to respond to fresh orange juice, a standard preparation should be substituted. Radiological changes (calcified subperiosteal hæmatoma) may be recognisable for many months after clinical recovery is complete.

Prognosis.—This is good if the condition is recognised early and promptly treated, but infants suffering from scurvy are particularly liable to develop intercurrent infection, and may occasionally die from hæmorrhage before the deficiency has been made good.

RICKETS

Ætiology.—Rickets is due to a deficiency of vitamin D, and is essentially a disease of the growth period. Vitamin D can be supplied in the diet, *e.g.*, fish-liver oils which are rich in this substance, or in synthetic preparations,

or it can be manufactured in the skin by the action of ultra-violet light when the precursor ergosterol is available. Lack of vitamin D results in failure of absorption and utilisation of calcium and phosphorus ; a similar disturbance may be produced experimentally by diets grossly abnormal in their calcium-phosphorus content. Failure of absorption of calcium is not typically reflected in a diminution of the calcium of the blood serum, since up to a certain point the deficiency is counteracted by withdrawal of calcium from the skeleton and its mobilisation ; when this mechanism breaks down and the serum calcium falls below approximately 6 mg. per 100 c.c., tetany (*vide* p. 187) results. The plasma inorganic phosphorus, however, is much more commonly diminished in rickets (*e.g.*, from a normal value of $5 \pm 0{\cdot}5$ mg. in infancy to one of 2 or 3 mg. per 100 c.c.), whilst in the active phase the phosphatase content of the blood is raised. A useful formula is the multiple of the serum calcium and plasma inorganic phosphorus contents of the blood, when both are expressed in milligrams per 100 c.c. If the multiple is less than 30, it indicates active rickets ; if between 30 and 40, mild or latent rickets is usually present ; a multiple above 40 contra-indicates rickets. (The plasma phosphorus, however, may be reduced from other causes than rickets, such as pneumonia.) This disturbance of calcium-phosphorus balance is reflected in a disability of the growing bone to lay down calcium phosphate, with consequent failure and disorganisation of ossification.

Prematurity is a predisposing cause of rickets, the premature being liable to develop the disease earlier than the full-term infant unless adequately protected. Generalised infection, *e.g.*, congenital syphilis, is also a predisposing cause. Scurvy may coexist with rickets, if the diet is deficient in both vitamins C and D, but is otherwise unrelated.

" Late rickets " may occur in cœliac disease, the arrest of growth in this disease having delayed the appearance of symptoms until more active growth occurs in early childhood. Occasional cases of " vitamin D resistant rickets " are seen, the condition persisting into childhood unless arrested with enormous doses of vitamin D. Renal rickets is not strictly comparable to vitamin D deficiency rickets, and it is probable that here one of the ætiological factors is the raised inorganic phosphorus of the blood and its excretion into the gut ; absorption of calcium will then be interfered with, owing to the formation of insoluble calcium phosphate. Renal rickets also differs from vitamin D deficiency rickets in that the blood phosphorus is usually raised rather than lowered.

Since human breast-milk is, except under bad urban conditions, a better protection against rickets than is cow's milk, the disease is commoner amongst artificially fed infants ; the breast-fed infant may, however, develop rickets if the mother's diet and exposure to sunlight are deficient, or after weaning.

Regular exposure of the infant to sunlight or even " sky-shine " on cloudy days will protect against rickets except under urban conditions, where the smoke-pall over large cities is likely to filter off a disproportionate amount of the ultra-violet rays. Regular exposure of relatively small areas (*i.e.*, face, hands, and legs) is better protection than occasional exposure of the whole infant ; the window-glass commonly used will deprive sunlight of its efficacy. As would be expected, the disease is one predominantly associated with poverty and urban conditions. The prolonged use of

sweetened condensed milk in infant feeding is particularly liable to produce rickets, since the amount of carbohydrate in most proprietary brands is excessive. Cereal, and particularly oatmeal, has been shown to be rachitogenic unless calcium is liberally supplied in addition, *e.g.*, in milk. Although the severer manifestations of the disease are now seldom seen, the minor grades of rickets are still common, and since the disease is readily preventable it must be regarded as responsible for much unnecessary ill-health.

Morbid Anatomy.—The most characteristic changes are found at the growing ends of the long bones and costo-chondral junctions. Here there is a general expansion, shown radiologically to be due to cupping, which results clinically in enlargement of the epiphyses of the wrists and ankles, and in beading of the ribs. On section, the line of the epiphysis is found to be enlarged and irregular ; microscopically, there is complete disorganisation and irregularity of the cartilage columns, and no clear line of demarcation between the cartilage and area of new bone-formation. Masses of giant cartilage cells are seen invading the shaft of the bone, whilst osteoid tissue is irregularly formed and imperfectly calcified. Beneath the periosteum there is similarly an excess of imperfectly calcified osteoid tissue, which may be recognisable radiologically.

In addition to these changes, the whole skeleton shows rarefaction due to inadequate deposition of calcium and phosphorus, and bending or greenstick fractures of the long bones are frequently found. The skull in young infants may show areas of extreme rarefaction (craniotabes).

Clinical Features.—These are most readily recognised in the skeleton, though the infant is likely to show other evidence of disease. Thus the muscles are hypotonic, resulting in a failure to sit up or walk, the abdomen distended, recurrent bronchitis and the passage of green stools are of frequent occurrence, and often the infant will show an associated nutritional anæmia. Growth may be affected, but often rickets will occur in large overweight babies who have been wrongly fed.

The skull shows frontal bossing, and in infants where rickets has developed early, *e.g.*, prematures, there may be craniotabes present in the occipital region. This is an extreme thinning of the skull, which gives the impression of egg-shell crackling on pressure, or which may permit the whole area to be indented. Persistent patency of the anterior fontanelle will be seen in older infants, but owing to the variable size of the fontanelle in early infancy this sign is of little value before the age of twelve to eighteen months.

The thorax shows a variety of deformities, of which beading of the costo-chondral junctions (the " rickety rosary ") and a transverse groove at the insertion of the diaphragm (Harrison's Sulcus) are the most characteristic. The beading of rickets differs from that of scurvy in that the enlargement of the costo-chondral junction is more or less uniform, affecting both the rib and cartilage. Thoracic deformities are likely to be more marked when there have been frequent respiratory infections.

The limbs will show enlargement in the region of the epiphyses, particularly at the wrist and ankle. Bending of the long bones will result from weight carrying or pressure, the infant who has learnt to sit up but not walk often showing maximum deformity of the forearms owing to leaning forward on the hands, the infant who has learnt to stand showing either genu valgum or varum, or an acute angulation of the tibia at the junction of the lower and middle third.

Whilst all these deformities may be present in a severe case, a mild case of rickets may show only one or more, and biochemical examination or X-ray may be necessary to confirm the diagnosis.

Diagnosis and Differential Diagnosis.—The dietetic history will often suggest the diagnosis of rickets, and the characteristic bony deformities confirm it. Of these, beading of the ribs is particularly helpful. In cases of doubt, the wrist should be X-rayed, since the appearance of cupping and the lack of demarcation between bone and cartilage are characteristic. Estimation of serum calcium, plasma phosphorus, and phosphatase may be indicated, but calcium-balance estimations are not usually practicable.

Occasionally areas of softening of the skull are seen in non-rachitic infants, whilst the symmetrically placed congenital parietal foramina which occur in certain families are unlikely to cause confusion if their nature is suspected.

Congenital softness of the sternum and congenital "funnel sternum" (which also tends to have a familial incidence) should be distinguished from the deformities of rickets.

Achondroplasia is congenital in origin, and characterised by extreme shortening of the arms and legs, and a peculiar facies; the X-ray appearance in no way resembles that of rickets. Osteogenesis imperfecta and Morquio's disease (chondro-osteodystrophy) are readily distinguishable on X-ray, since both lack the characteristic rachitic cupping.

Prevention and Treatment.—From what has been said of ætiology, it will be realised that rickets can be readily prevented either by oral administration of vitamin D or regular exposure to sunlight or ultra-violet light or by a combination of the two. All artificially fed infants and breast-fed infants living under poor or urban conditions should be given the equivalent of three teaspoonfuls of pure cod-liver oil daily, starting at the age of three months (or earlier in the case of prematures). For infants who do not tolerate this amount of fish oil, a large number of concentrates are available. Larger doses (2,500 international units of vitamin D daily) are required for treatment, and this may be combined with exposure to ultra-violet light. Calcium should be supplied liberally throughout treatment. Gross deformities may require splintage or subsequent operation, but considerable reduction of the bony deformities will often occur with medical treatment alone.

TETANY

(*Spasmophilia*)

Whilst tetany may occur in the newborn (possibly from birth injury to the parathyroids), or from alkalosis (*e.g.*, following prolonged vomiting due to high intestinal obstruction or hyperventilation), the type of tetany which is commonest in infancy is that associated with rickets.

The ætiological factors involved are for the most part the same as those producing rickets, though it is not clear why some infants with active rickets develop tetany and the great majority do not. The distinguishing feature between the two groups is that whereas in most cases of rickets the serum calcium is maintained at normal levels, in tetany it falls commonly to below 6 mg. per 100 c.c. Dysfunction of the parathyroids and alterations

of alkali reserve have been variously incriminated. As in rickets, cases are most likely to occur in February and March, *i.e.*, following the months in which there has been least sunlight. Infection may serve to precipitate tetany in a rachitic infant.

Since the calcium ion has a sedative action on nervous tissue, reduction of ionisable calcium (of which reduction in total serum calcium is only a crude index) is followed by irritability.

Clinical Features.—The age-incidence is the same as that of rickets, and infants with tetany are likely to show rachitic manifestations. Latent tetany is probably considerably commoner than manifest tetany, and is likely to be recognised only by careful neurological examination, and confirmed by biochemical investigation. The classical symptoms of manifest tetany are carpo-pedal spasm, laryngismus stridulus, and convulsions.

Carpo-pedal spasms are tonic contractures of the hands and feet, in which the fingers are flexed at the metacarpophalangeal joints, but extended at the interphalangeal joints, the thumb being drawn across the palm and the wrist flexed and deflected to the ulnar side. The feet are extended and the first phalanges of the toes are flexed. These spasms may be induced by firm constriction of the arm or leg (Trousseau's sign).

Laryngismus stridulus is a characteristic crowing noise on inspiration, brought out by crying, and due to a partial spasm of the glottis. It may be sufficiently severe to produce cyanosis, or precipitate a convulsion, but is very seldom fatal.

Generalised convulsions are often the symptom which first draws attention to the disease ; whilst these convulsions show no distinguishing features from convulsions due to other causes, the occurrence of a convulsion in a rachitic infant should suggest the diagnosis of tetany.

Examination of the infant is likely to show, in addition to Trousseau's sign, the presence of nervous irritability manifested by a twitch of the corner of the eyelid or lip on tapping over the facial nerve (Chvostek's sign). Electrical stimulation, *e.g.*, of the peroneal nerve, will demonstrate an abnormally increased sensitivity to the cathodal opening stimulation (Erb's sign).

Diagnosis.—The occurrence of the three classical symptoms in an infant with active rickets, confirmed by one or more of these three signs (Trousseau's, Chvostek's, and Erb's), will establish the diagnosis on clinical grounds. Estimation of serum calcium should be coupled if possible with an estimation of alkali reserve.

Treatment.—The immediate requirement of the infant is for ionisable calcium, and this is rendered available by the immediate administration of calcium chloride or ammonium chloride in dosage of 15 to 40 gr. (the chloride ion here being the effective principle). This should be followed by oral administration of calcium gluconate or lactate in doses of 15 gr. four-hourly, and after the immediate symptoms have subsided, by anti-rachitic therapy. Calcium gluconate may also be given intravenously (10 c.c. of a 10 per cent. solution). Sedatives, such as chloral hydrate, or even general anæsthesia, may be required as an emergency measure to control convulsions, but are no substitute for the correction of calcium metabolism.

PINK DISEASE

(*Acrodynia*)

The ætiology of this disease is entirely unknown, though many possible causes have been suggested. Since it shows certain similarities to a deficiency disease, intensive therapeutic tests have been made, particularly with the vitamin B complex, but so far the results have been entirely inconclusive. The great majority of cases occur in infants aged one to three years, but the disease has also been described in infants during the first months of life and in older children. The disease has been known to assume an epidemic character, and in general is commoner in the spring and early summer.

Morbid Anatomy.—Although patients sometimes die without explained cause or from intercurrent infection, particularly pneumonia, post-mortem examination has added very little to our knowledge of the disease. The clinical signs and symptoms suggest that the autonomic nervous system is affected, but there is singularly little neuropathological confirmation of this, the cases which have been studied histologically having shown no consistent changes in the nervous system or elsewhere.

Clinical Features.—The disease varies greatly in severity and duration. Typically, a period of anorexia, irritability, and loss of weight ushers in the classical symptoms of sweating, photophobia, and coldness and pinkness of the extremities. Skin rashes of varying character are commonly seen at any stage of the disease. In severe cases the extremities and nose may become cyanotic ; the hands and feet are intensely irritating, and the skin may become ulcerated from continual rubbing on the bed-clothes, or thickened and œdematous. The palms and soles commonly show peeling. The knee jerks are usually first diminished and then absent, whilst there is such marked general hypotonia that the child is unwilling or unable to walk. Loss of teeth without obvious cause is liable to occur in the severer cases. There is tachycardia and frequently some rise in blood pressure.

Throughout the disease, anorexia and photophobia persist, the latter causing the child to take up peculiar attitudes with the face hidden in the bed-clothes. Anorexia may result in a condition of severe marasmus.

Diagnosis.—The combination of profuse sweating, anorexia, photophobia, and discoloration of the extremities should leave no doubt as to the diagnosis if the disease is borne in mind.

Treatment.—The administration of vitamin B complex and liver is usually advocated, though there is little convincing evidence that it is of benefit. Since the main disturbances are anorexia and loss of sleep due to the pain and irritation of the extremities, treatment must be largely symptomatic. Careful nursing, sedation, relief of pain, and prevention of cross-infection are most important.

Prognosis.—The course of the disease varies from weeks to many months. If nutrition can be maintained and infection prevented, recovery is usually complete, though if trophic ulcers have formed on the extremities or teeth have been shed with subsequent infection of the mouth, permanent scarring or necrosis of the jaw may result.

CHRONIC INTESTINAL INDIGESTION

Under this heading may be included a number of intestinal disorders characterised by a varying degree of failure to absorb or digest fat, carbohydrate, or protein. All are likely to be associated with malnutrition, distension of the abdomen, and abnormal stools.

Fibrosis of the Pancreas

This has recently been separated as a distinct disease entity. The condition is congenital and may be familial ; it has been suggested that it is probably inherited as a Mendelian recessive. Both sexes are affected.

Morbid Anatomy.—The pancreas shows advanced fibrosis, with dilatation of the ducts and acini which has caused the condition to be described as " cystic fibrosis," though it has been pointed out that no true cysts occur. Associated with the pancreatic fibrosis are pneumonic or fibrotic changes in the lung. Bronchiectasis is likely to occur in older infants.

Clinical Features.—The intestinal symptoms are due to failure of normal secretion of pancreatic enzymes, secondary to the extensive fibrosis ; the function of the islets of Langerhans is not significantly disturbed. Infants may die during the neonatal period from *meconium ileus*, whilst those that survive are likely to show symptoms at an early age. The stools are more bulky than normal and contain an excessive amount of fat. This is normally split, probably by a lipase of the succus entericus. In spite of voracious appetite the infants commonly fail to gain weight, and wasting and abdominal distension become progressively more marked. In some cases, however, the effects on growth and nutrition are minimal. Respiratory symptoms are variable, the infants sooner or later showing chronic cough and often clubbing of the fingers. Death is frequently the result of a terminal pneumonia.

Diagnosis.—Whilst the clinical picture of wasting, fatty stools, and good appetite should suggest the disease, particularly when respiratory signs or symptoms occur in association with the intestinal ones, the diagnosis rests on the estimation of trypsin in the duodenal juice. The absence of trypsin confirms the diagnosis of fibrosis of the pancreas, whilst its presence in normal amount contraindicates it.

Treatment.—The child should be allowed a liberal diet, including predigested foods, *e.g.*, hydrolysate of casein, and pancreatin should be administered in large doses. As this latter is inactivated by the acid stomach-content, its potency is not reliable. Penicillin should be employed where there is active pulmonary infection.

Prognosis.—Although the general nutrition can be improved with treatment, the disease is liable to prove fatal owing to pulmonary infection.

Cœliac Syndrome

This is less clearly a distinct disease entity than is fibrosis of the pancreas, but the clinical picture is sufficiently characteristic to justify separate description ; it should be realised that the syndrome is likely to be further subdivided when the ætiological factors are more clearly understood.

Unlike those of fibrosis of the pancreas, the symptoms of cœliac disease

seldom appear during the first six months of life, and are frequently delayed until the second year or even later. The child, who has previously appeared healthy, begins to have recurrent attacks of anorexia, during which there is loss of weight and the stools become bulky and offensive, and pale in colour. They are found to contain a great excess of fat, which may even represent 60 to 90 per cent. of the weight of the dried stool, or a more accurate fat balance experiment will show the percentage of fat absorbed to be substantially below the normal; the fæcal fat is normally split, as in sprue. These attacks become more frequent and severe, whilst wasting becomes more and more pronounced. In advanced cases there is very gross wasting of the limbs and buttocks, whilst the abdomen becomes increasingly distended. Transient œdema is common, and largely accounts for the sudden variations in weight which are a common feature of the disease. Unless the vitamin requirements are adequately covered, the infant is liable to suffer from latent rickets, which becomes manifest when growth occurs in early childhood. Before this time, arrest of growth may be almost complete.

During the attacks the infants become extremely irritable and miserable, which adds to the difficulties of feeding.

In the great majority of cases there is no family history of the disease, and no consistent ætiological factors can be demonstrated. The trypsin content of the duodenal juice is normal, and there appears to be an idiopathic failure of absorption of fat and to a lesser extent chronic starch-indigestion associated with a flat blood-sugar curve.

Since the digestion of protein is much less affected, treatment includes the prescription of a high protein, low fat and carbohydrate diet; predigested protein may again be found useful, whilst certain forms of carbohydrate, *e.g.*, overripe bananas and rusks, are better tolerated than others. All the vitamin requirements must be adequately covered, the fat-soluble vitamins being prescribed in concentrated form. Some cases have appeared to benefit from treatment with vitamin B and liver extract, but the results are generally not dramatic. Since some degree of anæmia, which may be microcytic, normocytic, or macrocytic in type, is commonly present, the infant should receive appropriate treatment, which may include blood transfusion. There is no evidence that folic acid benefits cases other than those showing macrocytic anæmia, which is the rarest type.

Prognosis.—Since the disease is always chronic and associated with severe malnutrition, many infants succumb to intercurrent infections. Those which survive are likely to show some permanent stunting of growth or even infantilism, whilst some at least pass on into the condition of idiopathic steatorrhœa of adults. In milder cases the failure of fat absorption apparently becomes spontaneously corrected in later childhood.

Cyclical Vomiting

Recurrent vomiting attacks in infancy and childhood are comparatively common, and may be due to such various causes as parenteral infection, appendicitis, volvulus, dietetic indiscretions, allergy, and migraine. Failure to distinguish the primary cause may be disastrous, and the finding of ketone bodies in the urine of a child who is vomiting should never in itself be regarded as providing a satisfactory diagnosis. Ketonuria develops readily in childhood, and it is simply evidence of incomplete metabolism

of fat, which may be due to starvation, excess of fat in the diet, liver dysfunction, or diabetes. It is unfortunate that the term "acidosis" is often used as though it were synonymous with ketonuria, and referred to as a primary disease.

The term Cyclical Vomiting is best restricted to those cases where the child develops vomiting attacks and ketonuria with exceptional readiness from nervous or dietetic causes, and where organic disease has been excluded. Such children are commonly intelligent and described as "nervous." In these, any exceptional excitement such as the prospect of a party or the beginning of term may precipitate vomiting; the same children often suffer from train or car-sickness. There is sometimes a family history of allergy or migraine, though the cases in which the attacks are themselves allergic or migrainous in origin can usually be distinguished as separate groups. It should of course be remembered that any child who is known to be subject to cyclical vomiting may at any time develop a vomiting attack due to an organic cause, *e.g.*, tonsillitis or appendicitis, and requires careful re-examination in each attack.

Clinical Features.—The condition is most commonly seen in children over three, but may occur in later infancy. The vomiting is usually preceded by a short period of nausea, lassitude, and abdominal discomfort. Severe headache or visual disturbances during this period should suggest migraine. When the vomiting starts it is intractable for two or more days, and the child rapidly becomes prostrated and dehydrated. The blood-sugar may be low, but this is not a consistent finding. The ketonuria increases in degree, and the breath smells of acetone. The tongue is furred, the bowels constipated, and the urine reduced in amount and of high specific gravity. Upper abdominal pain is often a result of the severe and repeated vomiting.

Treatment.—The child should be put to bed in a darkened room. If the bowels have not been opened for twenty-four hours an enema should be given, and sedatives, *e.g.*, chloral and bromide, may be administered by rectum, since it is unlikely that they will be retained by mouth. Sips of sweetened orange juice or saline and glucose may be given by mouth, starting with 1 drachm half-hourly and doubling the dose as long as the fluid is retained. In some cases it will be found that dry toast and honey is better retained than fluids, but when dehydration cannot be overcome by administration of fluids orally it may be necessary to give 5 per cent. glucose in physiological saline intravenously. Sodium bicarbonate may be given in small doses (*e.g.*, 2 gr. two-hourly) by mouth, but there is a danger of the acidosis associated with starvation being converted into alkalosis if large amounts of alkali are given without control by estimation of alkali reserve and plasma CO_2.

After the attack, gradual return to a normal diet should be made, but fats should be restricted for at least a week. Between attacks, treatment must aim at avoiding the precipitating causes; if the tolerance for fats is low, these should be limited, though it is sometimes found that there is no decreased tolerance for fats between attacks, and that it is only when other factors have precipitated the attack that fat-metabolism becomes disordered. In general, these children require carbohydrate frequently throughout the day and do not tolerate long intervals between meals. Regular bowel action is important.

Prognosis.—This is good, although the condition causes frequent invalidism during childhood. The susceptibility to attacks usually diminishes greatly at or before puberty, though where they are migrainous in origin, typical migraine may persist into later life.

CONVULSIONS

Ætiology.—Convulsions in infancy are very much commoner than are fits or even rigors in adult life, due to the relative instability and immaturity of the infant's nervous system. They may be precipitated by a great variety of causes, and should be regarded as a symptom rather than a disease-entity. The most important causes are : (i) infection of the central nervous system or meninges, *e.g.*, tuberculous or meningococcal ; (ii) infection outside the central nervous system, any disease causing a sudden high rise of temperature (such as pneumonia, pyelitis, bacillary dysentery, or otitis media) being liable to precipitate a convulsion in a susceptible infant ; (iii) metabolic, *e.g.*, tetany, hypoglycæmia ; (iv) toxic, *e.g.*, lead, strychnine ; (v) intracranial tumours ; (vi) intracranial hæmorrhage and trauma, particularly birth injury ; (vii) congenital cerebral defect and degenerative processes ; (viii) idiopathic or epileptic. Not all infants of the same age are equally liable to secondary convulsions, and there is evidence that infants who develop convulsions readily are more likely than others to show epilepsy in later life. Thus peripheral irritation, *e.g.*, teething, is only likely to precipitate a convulsion in an infant who is already predisposed.

Morbid Anatomy.—This will depend on the primary cause. Convulsions *per se* may be associated with punctate hæmorrhages throughout the brain and congestion of the right side of the heart and of the lungs, but some fatal cases will show no recognisable changes.

Clinical Features.—Convulsions vary in severity from localised twitchings (often seen in the newborn) to generalised tonic spasms followed by clonic movements, deviation of the eyes, stertorous breathing, incontinence, cyanosis, and loss of consciousness. The duration again is very variable, the symptoms lasting a few seconds only or becoming semi-continuous, when the condition is similar to status epilepticus. Often the infant will first cry and then sleep on coming out of the attack, and may show subsequent transient paralyses.

Diagnosis.—Whilst a generalised convulsion is usually unmistakable, the diagnosis of the primary cause is likely to require detailed investigation, including examination of the optic discs and fundi, urine, ears, lungs, etc. The skull may show evidence of trauma, separation of the sutures, microcephaly, or other deformity. A lumbar puncture should be performed in cases of doubt, though this should never be done during a convulsion, and if there is any suspicion of there being a space-occupying lesion within the skull, fluid must only be withdrawn extremely slowly and in small amount. A Wassermann reaction may be required to exclude congenital syphilis. In selected cases electro-encephalography will be of help in establishing the diagnosis, or air-encephalography in determining the site of an intracranial lesion. In all cases a careful history should be taken, with particular reference to delivery, maturity, trauma, diet, and previous mental and physical progress. A family history may reveal hereditary factors.

Prognosis.—Since this depends on the primary cause, no general prognosis can be given. A history of repeated convulsions over a long period suggests that the condition is firmly established. If, however, the convulsions can be controlled with sedatives, the prognosis improves with the length of time over which the infant remains free from them.

Treatment.—Immediate treatment aims at arresting the convulsions. Placing the infant in a warm bath is a time-honoured remedy which does no harm. Sedatives (chloral and bromide or $\frac{1}{4}$ to $\frac{1}{2}$ gr. phenobarbitone) may be given by mouth between convulsions, or rectally if the drug cannot be retained orally. Similarly, 50 to 150 c.c. of 50 per cent. magnesium sulphate may be given rectally. If the infant has passed into status epilepticus, ether anæsthesia may be necessary.

Subsequent treatment will depend on the primary cause, but if repeated convulsions have occurred over a long period it is advisable to continue sedation for at least a year after the infant has been free from them. The drug used will have to be varied with the individual case. Chloral and bromide are relatively safe drugs to use in infancy (if watch is kept for signs of overdosage), and phenobarbitone in small doses is also usually well supported. Epanutin is, in the author's experience, rather more liable to produce toxic symptoms (dizziness and ataxia) in children than in adults, and if this drug is used the child should be kept under observation and the parents warned to be on the watch for evidence of overdosage. Some cases respond dramatically to this drug when the others mentioned have been ineffective.

Richard W. B. Ellis.

POISONINGS AND INTOXICATIONS

LEAD POISONING

LEAD may be absorbed through the lungs or through the alimentary tract. Inhalation of dust containing lead is a far more potent cause of poisoning than is absorption through the digestive tract. Specially dangerous occupations are those in which the workers are subjected to fumes from molten lead, or where they are exposed to the inhalation of air laden with dusty lead compounds (*e.g.*, lead carbonate or lead oxide). Occupations such as white-lead manufacture, smelting of metals, accumulator-manufacturing, and ship-breaking show the highest incidence of lead poisoning. Apart from such occupational risks, occasionally cases arise from the continued ingestion of a soft drinking water that has stood in lead pipes or cisterns.

As with all other poisons there is considerable variation in susceptibility. Certain factors predispose to the disease. Perhaps the chief of these is chronic alcoholism, while renal disease, gout, anæmia, and acute infections all render persons exposed to lead absorption specially liable to develop poisoning. After infections, exposure to lead should be avoided for at least a month. Women are rather more susceptible than men, and the young more susceptible than the mature.

Lead is mainly excreted into the colon and may be found in the fæces, whether the metal is swallowed or inhaled. To a less extent excretion takes place through the kidneys.

Acute Lead Poisoning.—This usually results from the swallowing of a large quantity of a soluble lead salt such as the acetate. There is a burning taste in the mouth and acute abdominal pain, accompanied by vomiting and diarrhœa. The blood pressure falls and signs of collapse develop. Death may occur within a few days, but frequently the patient survives and shows symptoms of chronic lead poisoning.

If seen within a few hours of swallowing the poison, the stomach should be washed out with dilute hydrogen sulphide water slightly acidified with sulphuric acid, as this tends to render the lead less soluble. Sodium or magnesium sulphate should be given in $\frac{1}{2}$-oz. doses in order to aid elimination from the bowel.

Chronic Lead Poisoning.—Early diagnosis is of the greatest importance. Among the early symptoms of plumbism are the following, any of which, should they occur in a person exposed to lead, must arouse suspicion :—

1. *Anæmia.*—Anæmia of varying degree is common in lead poisoning. The hæmoglobin percentage is 70 or below, and the colour-index is low. Basophil granules are seen in many of the red cells, a condition described as *punctate basophilia.* Although found in other forms of anæmia, it is rarely seen to such a striking extent as in lead poisoning. Its occurrence in a lead worker, even in the absence of other signs, is a valuable indication that lead absorption is occurring.

2. *Blue Line.*—In the presence of oral sepsis the well-known "blue line" appears near the gum margin. On careful examination with a lens the line is seen to consist of a large number of discrete granules of dark colour deposited deeply in the tissues. It is usually less than 1 mm. in width, and is specially obvious where oral sepsis is most marked. It does not occur at the exact point where the gum is adherent to the teeth, but is separated slightly from the gum margin. Care must be taken to differentiate the bluish coloration seen in pyorrhœa alveolaris from the blue line of plumbism, which is due to the formation of lead sulphide in the gums. It is produced by the action of sulphuretted hydrogen, derived from decomposition processes in the debris of protein food around septic teeth, on circulating lead. No blue line is seen if the mouth is edentulous, and care of the teeth reduces the liability to its occurrence. It must, however, be clearly understood that a blue line is nothing more than an index of recent lead absorption and is not in itself evidence of lead poisoning. A somewhat similar "blue line" also occurs following the taking of bismuth.

3. *Loss of Weight.*—This is due to a loss of subcutaneous fat, and to a less extent to wasting of the muscles.

4. *Abdominal Symptoms.*—Apart from lead colic, vague gastric symptoms, anorexia and particularly constipation are common in all stages of plumbism.

5. *Early Mental Changes.*—Mental lethargy and drowsiness are not uncommon in the early stages of lead poisoning. In other cases the patient is restive and irritable. He may complain of slight headache and of extreme fatigue.

6. "*Rheumatic*" *Symptoms.*—Vague pains in the muscles and around the joints occasionally occur.

7. *Neurological Symptoms.*—A fine tremor of the outstretched fingers, sometimes with formication and numbness, may occur early. It is often possible by careful examination to detect some slight weakness of the extensor muscles, especially of the ring and little fingers, many months before the typical wrist-drop appears.

Symptoms such as those described above may persist for long periods without producing serious disability. At any time, however, such patients are liable to display additional and more serious symptoms, the so-called "Toxic episodes." These are colic, palsy, encephalopathy, and ocular disturbances. Of these colic and palsy are by far the most common, colic occurring in practically every case and palsy in about 10 per cent. of cases.

1. *Lead Colic.*—The patient complains of severe abdominal pain, which is usually referred to the lower abdomen. Obstinate constipation and anorexia are also present. During the attacks of colic the pulse is slow and the temperature subnormal; firm pressure on the abdomen tends to relieve rather than to increase the pain. There is no rigidity, but sometimes firm tumours consisting of contracted intestine may be felt. Occasionally, difficulty may arise in differentiating the case from acute abdominal conditions.

2. *Lead Palsy and Encephalopathy.*—These are described elsewhere (*vide* p. 701).

3. *Ocular Disturbances.*—Toxic amblyopia with temporary blindness, but without obvious retinal changes, may occur. Peripheral neuritis involving the oculo-motor nerves may produce diplopia.

4. *Sequelæ.*—Some doubt has recently been expressed, particularly by American workers, concerning the time-honoured statement that chronic

lead poisoning produces arteriosclerosis and chronic nephritis. Much of the evidence on this point is contradictory, but the excellent work of Nye in Australia (*vide* p. 542) has shown beyond any doubt that, in children at any rate, chronic lead poisoning may lead to severe renal damage of the diffuse vascular sclerotic type. In women, plumbism often produces abortion, while in males there may be sterility.

Differential Diagnosis.—As a rule the occupation of the patient will suggest the diagnosis, but it must be remembered that abdominal symptoms in lead workers are not necessarily due to lead poisoning.

Prophylaxis and Treatment.—Industrial lead poisoning is notifiable in Great Britain to the Home Office. Its incidence has fallen as the result of preventive measures from 1,058 notified cases in 1900 to ninety-six in 1938. It is therefore at the present time a relatively rare disease.

The methods adopted for the prevention of lead poisoning fall under three main headings : (i) the avoidance of the ingestion of lead by the mouth ; (ii) adequate ventilation of workshops ; (iii) periodical medical examination of lead workers. The first of these can be attained by adequate provision of washing facilities and dining-rooms for workers. The second is unfortunately a more difficult problem ; in many occupations lead fumes and dusty lead compounds are inevitable, but the provision of local exhaust fans or the use of respirators may help to diminish their inhalation. As regards periodical medical examination all lead workers should be examined at least once a month ; special attention must be directed to the detection of loss of weight, constipation, a blue line on the gums, anorexia, anæmia, and weakness of the extensor muscles of the upper limbs.

When lead poisoning has developed, the first essential in treatment is the removal of the patient from the work in which the disease has been contracted. In mild cases this is sufficient. In all cases of fully developed poisoning a permanent change of occupation becomes necessary, as otherwise, relapse is certain to occur. Attention must be paid to the general hygiene of the patient, particularly as regards open air and sunshine, and the condition of the teeth and gums. Constipation is almost invariable, and is best treated by full doses of magnesium or sodium sulphate.

Following lead absorption the metal is stored mainly in the bones, and during the active stages of lead poisoning an attempt should be made to prevent the mobilisation of the poison from such storage. This may be effected by giving 3 pints of milk daily together with a vegetarian diet. Only after all acute symptoms have passed off should a cautious attempt be made to promote the elimination of lead. Potassium iodide may be given in small doses, not more than 5 gr. thrice daily at the beginning of treatment, as occasionally it appears to produce a temporary aggravation of symptoms. A far more effective method is to prescribe a calcium free diet and further to assist elimination by producing an acidosis with ammonium chloride (15 gr. eight times daily). This de-leading treatment should be continued for three weeks.

In cases of colic, hot applications to the abdomen give some relief, and the patient may be given an inhalation of amyl nitrite or $\frac{1}{100}$ gr. of atropine hypodermically. The administration of calcium gluconate is even more effective. In severe cases 15 c.c. of a 20 per cent. solution may be given by slow intravenous injection. This usually eases the acute pain. The constipation must be relieved, and for this purpose enemata are often required. For

lead palsy the wrists should be kept at rest on splints in a position of dorsiflexion, and massage and electrical treatment should be employed. In cases of encephalopathy, sedatives such as bromides and chloral are often necessary, and calcium gluconate may be given intravenously; in comatose patients, or those with convulsions, venesections or lumbar puncture are occasionally beneficial. For the anæmia the most useful measures are fresh air, plenty of fresh fruit and green vegetables, together with the administration of iron.

ARSENICAL POISONING

Arsenic was for long one of the most popular poisons employed by murderers, but at the present time it is seldom used, owing to the ease with which it can be recovered from the body of the victim, even long after death. Arsenical poisoning still occasionally occurs as an occupational disease, and as the drug is often employed as a poison for vermin and insects, accidental poisoning is sometimes encountered. Strict regulations limiting the amount of arsenic in foods and beverages have completely abolished poisoning from this cause.

Acute Arsenical Poisoning.—The most prominent symptoms are intense abdominal pain, diarrhœa, and collapse, and death may occur within a few hours. The stomach must be washed out and a solution of ferric hydrate introduced. Intravenous saline and morphia may be necessary.

Chronic Arsenical Poisoning.—This results from long-continued small doses of arsenic. The two most characteristic features are peripheral neuritis and changes in the skin. The neuritis, like that produced by alcohol, affects the legs rather than the arms; sensory symptoms are more prominent in arsenical neuritis, and numbness and pain in the legs are commoner than in alcoholism.

There is a brown pigmentation of the skin, which is specially marked in the flexures. The soles and palms show great thickening of the epidermis and appear dry and scaly, a condition known as hyperkeratosis. Unlike Addison's disease, arsenic does not produce pigmentation in the mouth.

Anæmia of a hypochromic type occurs in severe cases and there may be anorexia, gastric disturbances, and a tendency to attacks of diarrhœa.

The diagnosis in patients who are known to be taking arsenic is usually easy. Confirmation is obtained by the discovery of arsenic in the urine, fæces, or hair. There is no specific treatment. The absorption of arsenic must be stopped and elimination promoted by keeping the bowels freely open.

The inhalation of *arseniuretted hydrogen* (arsine) produces hæmoglobinuria, anæmia, and hæmolytic jaundice which may prove rapidly fatal.

Poisoning by Salvarsan and Allied Arsenical Compounds is described elsewhere (*vide* p. 131).

MERCURIAL POISONING

Mercurial poisoning is rare as an occupational disease, and in its acute form mainly occurs in attempted suicide. Medicinal treatment with mercury may lead to symptoms of poisoning.

Acute Mercurial Poisoning.—Rapid onset of abdominal pain and vomiting is followed by a hæmorrhagic diarrhœa. There is a metallic taste in the mouth, with profuse salivation. The kidneys are affected early, and anuria or uræmia supervenes.

Immediate treatment consists in washing out the stomach and the introduction of the whites of four eggs in a pint of milk, with a view to the formation of an insoluble mercury albuminate. Collapse is treated by warmth and stimulants, but when the pain is acute, morphia is required.

Chronic Mercurial Poisoning.—Pallor, loss of weight, headaches and indigestion are early symptoms of mercurial absorption. The most characteristic features of chronic poisoning are stomatitis and gingivitis with excessive salivation, albuminuria, and muscular tremors ("hatter's shakes"). The diagnosis can be confirmed by the finding of mercury in the urine.

Treatment consists in preventing the absorption of further mercury and promoting elimination through the bowels with saline purgatives.

CARBON MONOXIDE POISONING

Carbon monoxide (CO) poisoning may result from the inhalation of coal gas or the exhaust of petrol engines. While usually suicidal in origin, accidental poisoning is not uncommon. The poisonous effects of carbon monoxide are due partly to a specific toxic effect on the tissues, partly to anoxia, as the gas forms a stable combination with hæmoglobin, known as carboxy-hæmoglobin, thereby interfering with the action of hæmoglobin as an oxygen-carrier.

If the concentration of carbon monoxide in the inspired air is ½ to 1 per cent., death may occur within a few minutes. With high concentrations the patient rapidly becomes comatose and convulsed. Owing to the formation of carboxy-hæmoglobin the blood, skin, and mucous membranes are cherry-red in colour. Sometimes the patient may die suddenly of heart failure, particularly if the gassed patient exerts himself.

Prolonged exposure to carbon monoxide in low concentrations may produce chronic poisoning, and the patient may have fainting attacks, loss of power on exertion, headache, nausea, palpitation, or neuritis.

Prophylaxis and Treatment.—Canaries are extremely susceptible to very small amounts of the gas. When gas is suspected, as in mine shafts or caves, a canary is taken down, and so long as it remains unaffected the atmosphere may be regarded as safe.

In the treatment of carbon monoxide poisoning it is important to give oxygen to which 7 per cent. of carbon dioxide has been added. The latter stimulates the respiratory system and produces increased pulmonary ventilation. In severe cases an oxygen tent should be used. If the patient has ceased to breathe, immediate artificial respiration must be performed. This should be continued for at least three hours before giving the case up as hopeless. The tongue should be held forward and a free airway ensured. Venesection followed by blood transfusion may increase the oxygen-carrying power of the blood.

FOOD POISONING

A considerable proportion of the diseases to which man is subject are the result of eating infected or poisonous food, and were the term food poisoning taken in its widest sense it would include many maladies such as cholera, typhoid, dysentery, and some forms of tuberculosis. Food poisoning, however, has come to be used in a more restricted sense, and includes only certain types of gastro-intestinal infections and the results of ingesting poisonous substances such as certain fungi. Formerly the term ptomaine poisoning was used synonymously with food poisoning, owing to the idea that the symptoms produced by contaminated food were due to ptomaines, organic bodies resulting from the breakdown of protein. Ptomaine poisoning as a medical term is going out of use, as it is now realised that the decomposition products of food contaminated by non-pathogenic organisms are seldom injurious to man.

Food poisoning may be classified into two main groups of cases : (i) poisoning due to chemical bodies, as, for example, in certain fungi and fruits ; (ii) infection of food by certain pathogenic organisms, which may produce toxins in the food before it is eaten, or may multiply within the body.

Food poisoning of the first group is relatively uncommon and usually results from eating poisonous fungi in mistake for mushrooms. Soon after ingestion of the poisonous material, vomiting, diarrhœa, and collapse occur. The liver is often affected, and a condition resembling acute hepatic necrosis supervenes with a fatal result (*vide* p. 341).

Far more important, however, is food poisoning due to the infection of food by pathogenic organisms, particularly *B. ærtrycke*, *B. enteritidis* of Gaertner, and *B. dysenteriæ Sonne.*

Contamination of food depends on a number of factors. One of the most important of these is the climate. In hot countries food poisoning is notoriously common owing to the fact that micro-organisms can multiply rapidly, and also because the food is more liable to become infected by flies. Lack of care in the preparation and storage of food will increase the danger of food poisoning, as will also the length of time during which food is kept before consumption. Food poisoning is often supposed to be associated with the use of canned food, particularly meat and fish. With modern methods of sterilisation in the canning industry the risk is negligible.

Food Infection by the Bacillus Dysenteriæ Sonne. *B. dysenteriæ Sonne* is frequently the cause of localised outbreaks of diarrhœa and vomiting in adults and of diarrhœa in children (*vide* p. 180).

The clinical course varies greatly : in the majority diarrhœa and vomiting are associated with moderate fever of some twenty-four to forty-eight hours' duration. Others have milder symptoms for some weeks. A simple fluid diet with rest in bed is usually all that is required. The organism quickly dies out in the majority of cases. Personal hygiene is essential to prevent the spread of infection, and, in institutional epidemics, search should be made for a carrier.

Food Infection by the Gaertner Bacillus and Allied Organisms.—The symptoms vary considerably in severity, ranging from a mild attack of vomiting and diarrhœa to a condition of profound and sometimes fatal collapse. The virulence of the organism, the amount of contaminated food eaten, and

the reaction of the individual are all important factors in determining the course of the illness.

The onset of symptoms is usually within a few hours of the ingestion of the infected material. The earliest to appear are dizziness and abdominal pain of a colicky character; nausea and vomiting occur early, and later there is diarrhœa with the passage of watery stools. In mild cases, when the infected food has been got rid of by vomiting or diarrhœa, the patient rapidly recovers. In severe cases, however, there are grave constitutional symptoms. After a few hours there is some degree of pyrexia, and the repeated vomiting and diarrhœa produce a condition of tissue dehydration which may resemble cholera. As in the latter disease, the stools are rice-water in type, with no fæcal material; rarely blood and mucus may be passed, suggesting bacillary dysentery. The facies becomes pinched and the eyes sunken; severe cramps, as in cholera, occur in the calves; the urinary flow is diminished owing to dehydration, and eventually the patient may die of cardiac failure. Needless to say, all grades of severity occur between the very mild and very severe choleraic forms of the disease.

A diagnosis of food poisoning should not be made without a careful physical examination to exclude appendicitis and other abdominal conditions. Frequently the occurrence of symptoms among a number of people who have partaken of the same food will give a clue to the diagnosis; but it must be remembered that individuals vary greatly in their susceptibility to food poisoning, and therefore not every one who has eaten infected food need necessarily show symptoms. Those who have previously suffered from dysentery or colitis are specially susceptible.

The treatment will vary with the severity of the illness. Confinement to bed is advisable during the acute stage. In most cases rest in bed with tinct. opii (25 minims) or kaolin ($\frac{1}{2}$ to 1 oz.) produces a rapid cure. A hot-water bottle on the abdomen usually relieves the colic. Nothing should be given by mouth except water or albumin water with a little glucose. In severe cases with dehydration and collapse, the first essential is to restore the fluid content of the body, and this may be done by rectal salines. If the latter cannot be retained, intravenous saline may be necessary. In severe cases convalescence is slow and the patient may develop a chronic gastritis, which may need careful dietetic treatment for many months. In mild cases, when the acute symptoms disappear, rapid return to a normal diet is possible.

Botulism.—This exceedingly rare disease is due to the toxins of *Clostridium botulinum*, an anaerobic spore-forming bacillus contaminating tinned food. The symptoms resemble those of an encephalitis rather than food poisoning. The prominent features are diplopia, ptosis and failure of accommodation, progressive muscular weakness, constipation, and respiratory failure.

Treatment, usually ineffective, consists in immediate administration of antitoxic serum (obtainable from the Ministry of Health), some form of respirator apparatus, and small doses of morphine.

Food Idiosyncrasies.—Hypersensitiveness to the protein in certain kinds of food is not uncommon. Such articles of diet as shell fish, milk, eggs, and strawberries may in certain individuals produce urticarial rashes and sometimes attacks of diarrhœa and vomiting. The specific nature of the reaction may be proved by cutaneous reaction tests with proteins derived from various articles of food. In some cases asthma may be due to sensitisation to food

proteins. As a rule the patient discovers for himself the substance which produces symptoms and avoids it. Sometimes it is possible to desensitise by the injection of repeated small amounts of the proteins concerned.

BROMIDE AND BARBITURATE POISONING

Bromide Intoxication.—Bromides, if taken in large amounts over a long period, may be retained in the body and produce confusion, disorientation, hallucinations, and delusions. The reflexes are sluggish and there may be tremor and ataxia. The patient may even become stuporous. The well-known bromide rash, resembling acne, is not commonly seen in these cases. If it is not known that the patient has been taking large amounts of bromide, the symptoms may be mistaken for other toxic states such as chronic alcoholism. The diagnosis can be confirmed by finding an excess of bromide in the blood. If this is above 100 mg. per 100 c.c. the symptoms are likely to be due to bromide. Rarely, owing to an idiosyncrasy, even small doses may produce symptoms.

Treatment.—Bromide should be withdrawn and the patient made to take large amounts of fluid. Elimination of bromide is effected by giving sodium chloride. This is best taken in cachets or pills containing 10 gr. at two-hourly intervals.

Barbiturate Poisoning.—These drugs include veronal, dial, nembutal, and phenobarbitone. Overdosage produces drowsiness, ataxia, tremor and stupor, and the patient is very liable to die of hypostatic pneumonia. In cases of acute poisoning, stomach and colon lavage may be beneficial, and strychnine and atropine should be given in full doses. Picrotoxin should be given intravenously in a 1 in 1,000 solution at the rate of 1 c.c. per minute. It has a stimulating effect on the cerebral cortex and the medulla. The drug is stopped when twitching of muscles occurs or when the corneal and pupillary reflexes return. Picrotoxin is dangerous in opium poisoning. Repeated lumbar puncture with drainage of the theca is of value.

ALCOHOLISM

The problem of alcoholism has always been one of the greatest difficulties which beset the way of both social reformer and doctor, and no attempt can be made here to discuss the wider aspects of the problem. Without doubt the ultimate solution will lie not in prohibition but in an improvement in social and economic conditions.

Alcoholism may be classed as acute and chronic. The first is sufficiently common to need no description. It is most important not to make a diagnosis of alcoholism in a comatose patient until other possibilities have been excluded. The smell of alcohol in the breath is of no diagnostic value, as sudden illness of all varieties is often treated by giving the patient brandy or other forms of alcohol. In case of doubt observation for a few hours will usually settle the diagnosis. Intramuscular coramine often hastens the return of consciousness in alcoholic coma. It is well to remember that hypoglycæmia (*vide* p. 239) may exactly simulate some of the stages of acute alcoholism.

A medical man may at any time be called upon to decide on the question as to whether a person is under the influence of drink while in charge of a car.

Special attention should be paid to the following points : (i) Test the memory for recent and past events, noting any abnormal emotional reactions and defects of speech. (ii) Test co-ordination in walking or standing with feet together, also ability to pick up an object, such as a coin. (iii) Obtain a specimen of handwriting, being careful to provide a good light and satisfactory material for writing. (iv) Take the pulse. This is usually rapid and full, but allowance must be made for nervous factors. (v) Examine the pupils. These are usually dilated and react somewhat sluggishly. (vi) Smell the breath, bearing in mind that a smell of alcohol is not in itself evidence of alcoholism. Under the Road Traffic Act of 1930 it is an offence to be " under the influence of drink or a drug to such an extent as to be incapable of having proper control of the vehicle." In view of the fact that the examining doctor may have to stand a rigorous cross-examination in court, he should be specially careful to make a thorough physical examination, making notes of his findings. Estimation of the alcohol content of the blood may be of value in doubtful cases. If this exceeds 2·4 parts per 1,000, it can almost certainly be assumed that the person was under the influence of alcohol in a legal sense. Lower concentrations, however, do not prove sobriety.

Chronic alcoholism is a more serious proposition, producing as it does widespread changes both in the viscera and nervous system and in the intellectual capacity of the patient. The organic changes which may be brought about by the continued use of alcohol include chronic gastritis, cirrhosis of the liver, arteriosclerosis and disease of the myocardium, chronic nephritis, and peripheral neuritis. Such lesions are not necessarily present in every case of chronic alcoholic poisoning, and for further details reference must be made to the sections on the diseases of the various systems concerned.

There are many factors in the ætiology of alcoholism. Heredity is certainly one, but direct inheritance of an alcoholic tendency is less common than might be imagined. Often the causes are occupational, as for instance in the case of bar-tenders, certain commercial travellers, or those employed in hot and dusty industries. The social surroundings also have a considerable effect on the individual ; sordid housing, monotonous work, domestic unhappiness, all tend to be factors in the production of chronic alcoholism. Most important of all, however, is a psychopathic tendency in the individual, who finds alcohol a ready means of escape from the difficulties and problems which face the ordinary man.

A large number of different alcoholic psychoses have been described, in some of which probably alcohol is but an incident rather than a cause, but there are four fairly well-defined conditions which need separate description. These are chronic alcoholism, delirium tremens, Korsakow's syndrome, and dipsomania.

Chronic Alcoholism.—In the more severe grades of chronic alcoholism the patient does not get drunk in the ordinary sense of the term, and he is often able to stand doses of alcohol which would produce manifest alcoholic symptoms in a normal person. The long-continued abuse of alcohol, however, produces a typical clinical picture. Irritability and a progressive deterioration in intellect and character become apparent, especially in the domestic circle ; among friends and strangers the chronic alcoholic may be tolerable enough, but in the bosom of his family he is quite prepared to make the life of those around him a misery by his callous disregard for the welfare of anyone except himself, his irritability, and sometimes even his violence. In his business or

profession the quality of his work deteriorates ; he is careless and unpunctual, and lacks the mental concentration necessary to complete an uncongenial task. Often only under the stimulus of alcohol is he able to carry on a normal life. Depression may alternate with excitement, and suicide is not uncommon. He has but little insight into his condition, and strongly resents any suggestion that his failings are due to alcohol ; he is suspicious, ready to see affronts and to pick quarrels. Sometimes there may be a paranoid reaction and delusions of persecution may arise. He is persistently untruthful, and promises to reform are invariably broken. Occasionally chronic alcoholism is encountered in persons who, at first sight, appear to be above suspicion. This is specially true of women at about the menopause, who may indulge in secret drinking.

Physically, many alcoholics are obese and plethoric, except in the later stages, when there may be marked loss of flesh. There is a coarse tremor of the hands, and tremor of the tongue and lips may render articulation difficult. Appetite is impaired and morning anorexia is often complete. The cardiac failure sometimes seen in alcoholics, especially in heavy beer drinkers, is probably due to lack of vitamin B (*vide* p. 254).

Delirium Tremens.—This well-defined condition may arise in chronic alcoholics as the result of a debauch, or in intercurrent infections, such as pneumonia ; fractures or sudden withdrawal of alcohol may also produce delirium tremens. The symptoms and treatment are described on page 759.

Korsakow's Syndrome.—This term is applied to cases in which there is a peripheral neuritis associated with a mental condition in which memory for recent events is lost, with marked disorientation (*vide* p. 760).

Dipsomania.—This condition is really a series of attacks of acute alcoholism, which tend to recur at more or less fixed intervals. Between the attacks the patient may be apparently a perfectly normal person and is often then a total abstainer, but with each attack comes an uncontrollable craving for alcohol, which must be satisfied at all costs. The condition is often hereditary and tends to develop in middle life. In character the attacks are probably allied to the manic-depressive type of insanity and the ultimate prognosis is bad.

Treatment of Chronic Alcoholism.—Before attempting treatment it is necessary to investigate the circumstances under which the condition has originated. If these are occupational, no attempt must be made to return to the work in which temptation occurred. Every effort must be made to gain the patient's confidence, and this is best achieved by regarding him not as a criminal but as the victim of a disease. In severe or long standing cases institutional treatment is a necessity, as otherwise it is impossible to ensure the patient giving up alcohol. At the beginning of treatment decreasing amounts of alcohol are allowed, until at the end of a fortnight the allowance has been cut down to nothing. After this, complete abstinence must be insisted on for the remainder of life. As alcoholism is so frequently psychological in origin, an attempt must be made to secure a readjustment of the patient's surroundings and general regime. No drug has any specific action, but in the early stages of the withdrawal of alcohol, bromides and chloral may be necessary to secure sleep.

The outlook in chronic alcoholism is usually poor, particularly when the alcoholism is but one symptom of an inherent mental instability. Even after prolonged institutional treatment relapse is frequent when the temptations and difficulties of normal life are again encountered.

MORPHINISM

Morphinism is less common than alcoholism, and produces less effect upon the general health. The drug, however, is more deleterious than alcohol in its effect on intellect and character. The compounds most generally employed are tincture of opium, heroin, and morphine. Of recent years the Dangerous Drugs Act has increased the difficulty of obtaining the drugs, but unfortunately the addicts of morphinism will go to any lengths to obtain a supply, and usually succeed in doing so.

Drug addiction, especially where the opium group is concerned, is seldom found except in individuals with a psychopathic inheritance, and it is doubtful whether there is ever any serious risk of the habit developing in a person with a normally stable nervous system. More often an exaggerated horror of drugs leads to the withholding of morphia and other sedatives in spite of indications for their administration.

In chronic poisoning by opium and its derivatives, physical health is often well maintained even when very large doses are being taken. As an example of this, a medical student was found to be taking 8 gr. of morphine daily and yet was able not only to carry on with his studies but also took an active part in athletics, such as boxing and football.

Perhaps the most significant change in character brought about by morphinism is the complete disregard of all conventional moral qualities, such as honesty and truthfulness. A morphia addict will without a qualm rob his best friend and, if discovered, feels no sense of shame. When under the influence of the drug the patient is often amiable and may appear normal, but as its effects wear off he becomes restless and irritable until relieved by the next dose. With complete withdrawal, delirium with hallucinations may occur. With long-continued use the dose needs to be progressively increased. Ultimately the general health may suffer, but the morphia habit is often consistent with a long life. This is especially true of the use of opium, which in many countries, such as India, is taken regularly by a large proportion of the population apparently without serious effects either on body or mind.

On physical examination the most obvious sign is myosis of the pupils; the reflexes are often diminished, and paræsthesiæ and hyperæsthetic areas are present. As the result of an overdose of morphia the patient lapses into coma, with a marked slowing of the respiration rate.

The *treatment* of well-established morphinism is most difficult, partly because the patients are usually the subjects of an inherent nervous instability. Relapse even after apparent cure is extremely common, and continued abstention from the drug is usually attained only by a difficulty in obtaining it. The prognosis is, therefore, especially bad among doctors and nurses, who can seldom resist the opportunities which fall in their way. The only satisfactory method of dealing with morphia addicts is strict confinement in an institution, where they can be prevented from obtaining access to the drug. Great care must be taken to ensure that the patient does not secrete a supply of the drug on his person before he enters the institution.

Sudden and complete withdrawal of the drug may produce dangerous collapse, especially in elderly and debilitated persons. It is best withdrawn gradually over a period of about fourteen days. For the restlessness and distress produced by abstention, large doses of bromide, chloral, or luminal

may be required. The bowels should be kept freely open to aid in elimination of the drug. In dealing with elderly addicts who have been taking the drug for years, attempts to withdraw the drug are more likely to shorten the patient's life than to lengthen it.

The permanence of cure depends mainly upon the patient being enabled to live a sheltered life. With exposure to financial, business, or domestic worries, or to physical or nervous strain, there is a grave risk of a return to drug-taking.

COCAINISM

Cocaine may be taken hypodermically, by mouth, or in the form of snuff, but the last method is that most frequently employed.

It has already been stated that morphinism seldom develops, apart from some psychopathic tendency. This is even more true of the cocaine habit, which is often started deliberately. Cocaine addicts, owing to the expense of the habit, are nearly all drawn from among the wealthy classes, but it may occur among the large number of agents who are engaged in the illegal distribution of cocaine. Anorexia is perhaps the most marked symptom. The cocaine addict can practically dispense with food altogether. Unlike morphia, cocaine is a stimulant, which produces a temporary sense of well-being and mental activity, but as the effects of the drug wear off there is depression and irritability until a further dose is taken. Morally there is rapid deterioration, and the unfortunate addict soon comes completely under the control of those who supply him with the drug, to obtain a supply of which he is ready to stop at nothing. Suicide is not uncommon, or death may occur from an accidental overdose. The emotional state varies between exultation and dejection; vivid and terrible nocturnal hallucinations are common. The pupils are dilated and the eyes have a sparkling appearance while under the influence of the drug.

As regards treatment, the first essential is that the confidence of the patient should be obtained, as without his co-operation it is almost impossible to prevent him obtaining the drug. A complete breach in the patient's relationship with other addicts and with the illegal traffickers in the drug is essential.

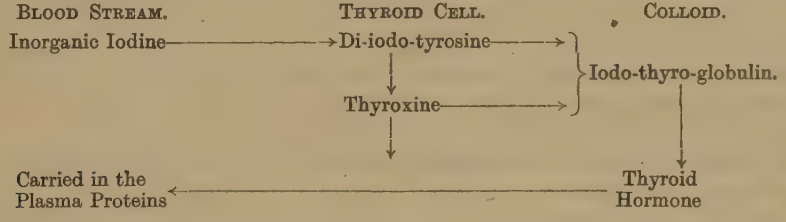
Unlike morphia, cocaine may be completely withdrawn at once, but the patient must be under close personal supervision, either in an institution or at home. If the craving for the drug becomes intense it may be relieved by giving hyoscine, preferably by mouth. The general health should be attended to by keeping the bowels freely open with salines and by exercise with plenty of open air.

J. J. Conybeare.

DISORDERS OF THE ENDOCRINE SYSTEM

THYROID GLAND

PHYSIOLOGY.—The thyroid gland is capable of utilising inorganic iodine supplied to it by the blood stream. This iodine combines with tyrosine in the epithelial cells of the gland to form di-iodo-tyrosine, some of which is converted to thyroxine. These two substances are then built up into the protein compound iodo-thyro-globulin for storage in the lumen of the thyroid vesicle as "colloid." The true thyroid hormone is probably an iodised albumin derived from iodo-thyro-globulin by a proteolytic process in the colloid. The conversion of di-iodo-tyrosine and thyroxine to iodo-thyro-globulin and its breakdown to thyroid hormone is probably brought about by a series of reversible oxidase reactions under the control of the thyrotropic hormone of the anterior pituitary, which is responsible, therefore, for the rate at which the thyroid hormone is supplied to the blood stream in which it is carried by the plasma proteins. Excessive stimulation of the gland by pituitary thyrotropin leads to acceleration of this rate, and is accompanied by increased activity of the thyroid cells, which grow in size and may multiply in number at the expense of the colloid, which practically disappears. This is the histological picture found in Graves' disease. On the other hand, diminished stimulation of the gland by the thyrotropic hormone leads to slower hormone production with a tendency to colloid storage and gives rise to the histological picture of the resting gland, large colloid vesicles bounded by flattened epithelial cells.



Though the thyrotropic hormone controls the rate of activity of the thyroid cell, its own output is in turn influenced by the amount of thyroid hormone circulating in the blood stream. When the concentration is high, thyrotropin secretion is inhibited, whereas deficiency of thyroid hormone leads to increased output of thyrotropic hormone. This pituitary-thyroid relationship plays an important part in the histological changes of the gland in simple goitre. In districts where there is deficiency of iodine in the water, simple colloid goitre is endemic. The lack of iodine leads to a diminished production of thyroxine, and thus to lowered concentration of circulating thyroid hormone. There is consequently increased output of pituitary thyrotropin resulting in hyperplasia of the thyroid cells. When from time to time, however, relatively increased supplies of iodine become

available they are immediately stored, with consequent accumulation of colloid and the formation of a colloid goitre. It has recently been shown that thiouracil can prevent the utilisation of the inorganic iodine of the blood. If administered in a case of Graves' disease there will be a consequent (and quantitative) decrease in the amount of thyroid hormone secreted into the blood stream; but, though the symptoms of the disease may abate, there will be no diminution in the overactivity of the thyroid cells which is due to a thyrotropic stimulus. Indeed the glandular hyperplasia may be accelerated on account of the diminished quantities of iodine being utilised.

Finally, in hypothyroidism, the glandular tissue is deficient in amount or in its responsiveness to the thyrotropic stimulus, with consequent diminution in the supply of the hormone to the blood stream. Quantitative deficiency may be congenital and lead to cretinism. Diminished responsiveness or actual cellular degeneration leading to myxœdema may take place at any age, though it most commonly follows such periods of physiological overactivity as pregnancy and the menopause and represents a condition of exhaustion atrophy. Histologically the gland may be largely replaced by fibrous tissue and it may even be difficult to identify the structure of the cells and vesicles.

GOITRE

(*Simple, Colloid, Endemic, Nodular, or Adenomatous Goitre*)

Goitre is endemic in mountainous districts and in areas far removed from the sea, such as Derbyshire, the Alps, the Himalayas, and around the Great Lakes in America. In these regions there is a deficiency of iodine in the water. Goitre may also occur sporadically in places where it is not endemic. Women are more commonly affected than men. The goitrous swelling frequently develops from the normal physiological enlargement of the gland which occurs at such times as puberty and during pregnancy.

The degree of enlargement is very variable, and though it may be considerable and unsightly it seldom produces symptoms. Dyspnœa and compression of the trachea, however, may accompany a very large thyroid or a retrosternal goitre. The latter may give rise to severe pressure symptoms.

The gland itself may be enlarged as the result of a generalised increase in the colloid substance in the alveoli, or there may be localised adenomatous enlargements in which cysts may develop. The condition is then termed cystic adenoma. Adenomatous enlargement of the thyroid may after middle life produce thyrotoxic symptoms. This condition is often termed secondary Graves' disease or toxic adenoma.

Treatment.—In endemic areas prophylaxis has proved most effective. Iodised salt or chocolate-coated iodide tablets are used in some districts. In others sodium iodide is given for a fortnight twice a year to all children. Each course consists of about 30 gr. Therapeutic administration of iodine in established cases of goitre has proved less effective, though it should be given a trial, especially in early cases: 15 to 30 minims of Lugol's iodine (iodine 5 per cent., pot. iodide 10 per cent.) is a suitable daily dose, or 5 gr. of potassium iodide daily is equally effective. Definite localised adenomata

are better treated surgically. Many adolescent goitres tend to disappear without treatment.

Carcinoma.—This condition is fortunately rare. It may occur spontaneously in a normal thyroid in middle age, or perhaps more commonly a carcinoma develops in an adenomatous goitre which has been present for many years. Surrounding parts are rapidly invaded, leading to fixation of the gland, enlargement of the adjacent lymph glands, and secondary deposits especially in bones. These metastases may contain active thyroid tissue and give rise to hyperthyroidism. The only effective treatment is early surgical excision of the thyroid tumour. Recently treatment with radio-active iodine has been tried but has so far proved disappointing.

Thyroiditis.—Acute inflammation of the thyroid may produce an abscess which requires drainage. Chronic inflammatory changes may also occur, known as *Riedel's thyroiditis* or " woody " thyroid. In this condition a small, hard, and often tender mass consisting of dense fibrous tissue is found in one lobe of the gland. Involvement of the recurrent laryngeal nerves may produce paralysis of a vocal cord and there is often pain on swallowing and referred pains in the chest and neck. The nature of the inflammatory process is unknown, and the condition is sometimes progressive in spite of thyroidectomy. This condition is to be distinguished from *Hashimoto's disease*, which consists of a diffuse lymphocytic infiltration of the gland followed by fibrosis, and usually giving rise to myxœdema. Pressure symptoms are not marked. Treatment is operative and recurrence is rare. Post-operative myxœdema is to be expected.

THYROTOXICOSIS

(*Exophthalmic Goitre, Graves' Disease, Hyperthyroidism, Toxic Adenoma*)

Morbid Anatomy.—The histological picture is one of general hyperplasia of the gland. The alveoli are variable in size, and there is little colloid to be seen. The alveolar cells are columnar and are arranged irregularly in multiple layers with the formation of papillary ingrowths in place of the single layer of cuboidal cells which lines the normally secreting alveolus. The amount of fibrous tissue increases as the condition becomes chronic. Lymphocytic infiltration is a prominent feature. In some cases the gland may show single or multiple adenomata in various stages of development or degeneration.

Enlargement of the thymus at autopsy is seen in about half the cases. Evidence of myocardial degeneration is rare even in patients dying of cardiac insufficiency.

Ætiology.—Thyrotoxicosis is frequently preceded by emotional strain. It occurs more frequently in women than in men. It presents a variety of clinical pictures depending on the age and previous make-up of the patient, picking out and emphasising the weaknesses of the patient's constitutional diathesis. It is probably due to increased secretion of thyrotropic hormone by the pituitary.

Symptoms.—In early adult life the onset of thyrotoxicosis may be sudden, but not infrequently in patients of middle age and over the onset is insidious, and such cases are liable to be misdiagnosed as heart disease or

neurasthenia. As the symptoms and signs vary considerably in every case, they are best considered separately.

1. *Thyroid Gland.*—The enlargement of the thyroid is very variable in extent, and the severity of the disease by no means coincides with the degree of glandular enlargement. Occasionally, indeed, there may be no obvious enlargement clinically, although the gland on section may show characteristic hyperplasia. The blood supply is much increased, and a systolic or continuous murmur, often very loud, may be heard over the gland; in severe cases a thrill may also be felt. The enlargement often involves both lobes and the isthmus, and the gland forms an obvious tumour in the neck, which can be seen to move on swallowing. In the earlier stages of the disease the thyroid is of normal consistency, but later on it may become unduly firm from an increase in fibrous tissue. This is often the case after treatment with iodine.

When thyrotoxicosis develops in a patient with an old-standing goitre, the gland is usually hard and nodular, but sometimes symptoms may arise when there is nothing beyond a very small and localised adenoma.

2. *Heart.*—Tachycardia is one of the earliest and most constant findings in thyrotoxicosis. The rate may range from 90 to 140 beats per minute, and under the influence of any excitement or emotion there is a rapid acceleration. The pulse pressure is high owing to a raised systolic pressure, the diastolic remaining normal. The heart is at first of normal size and the rhythm regular, but when tachycardia has persisted for a long period, especially in persons over middle age, dilatation, myocardial insufficiency, and auricular fibrillation may develop.

3. *Exophthalmos.*—Prominence of the eyes is a frequent though not invariable accompaniment of thyrotoxicosis. Even when of slight degree it is readily noticeable. The classical signs of exophthalmos, such as a lagging of the upper eyelid on looking downwards and a spasm or retraction of the upper lid with inability to blink are of little value in diagnosis. Occasionally exophthalmos may be unilateral.

Exophthalmos may be due to excessive secretion of thyrotropic hormone by the pituitary rather than to increased thyroid activity. If thyrotropic in origin it may persist or even become more severe after thyroidectomy, even though the patient is myxœdematous.

Exophthalmic ophthalmoplegia is a term applied to certain cases where in addition to exophthalmos there is paralysis or weakness of the external ocular muscles. In addition there may be chemosis and swelling of the eyelids. This syndrome may occur in thyrotoxic patients, but often there is little if any increase in thyroid activity. Thyroidectomy may aggravate the condition when it is of pituitary origin, as the thyroid exerts a restraining influence on the production of thyrotropic hormone. Thyroidectomy is therefore contraindicated in patients with exophthalmos with little or no other evidence of hyperthyroidism.

4. *Loss of Weight.*—In the more acute cases there is often a rapid loss of weight, but in the more chronic forms of the disease this is not necessarily a striking feature.

5. *Muscular Fatigue.*—This may be profound and in some cases of severe thyrotoxicosis the muscles are so atrophied and weak that the condition closely resembles progressive muscular atrophy. After thyroidectomy the muscles regenerate.

6. *Nervous Symptoms.*—Mental instability is always a marked feature, especially in younger patients. The patient is restless even when in bed, irritable, and very prone to be upset by small annoyances. Depression is common and weeping occurs without obvious cause. In severe cases the restlessness may amount to mania and delirium, and these symptoms are of grave significance. Tremor of the fingers is a constant feature, and is best seen when the hands are outstretched and the fingers separated. Unlike that of alcoholism, the tremor is fine in character and interferes but little with voluntary movements.

7. *Gastro-intestinal Symptoms.*—These are absent except during the exacerbations or " crises " of the disease. Vomiting and diarrhœa may be severe and intractable, and are of bad prognosis.

Some degree of impairment of liver function may be found in thyrotoxicosis ; this can be demonstrated by liver function tests.

8. *Skin.*—This is warm and moist and the patient often complains of feeling hot and of intolerance to hot weather. The hair may fall out and the skin is sometimes pigmented.

9. *Generative Organs.*—The menses may be scanty, irregular, or absent. During pregnancy, symptoms are sometimes temporarily improved, but relapse is apt to occur after parturition.

10. *Urine.*—Diminished sugar tolerance may result in glycosuria.

Basal Metabolic Rate (B.M.R.).—Estimations of the B.M.R. are of great value both in diagnosis and as a guide to progress under treatment, provided that the procedure is carried out with meticulous attention to detail. Casual estimations done by amateurs are worse than useless. The rate of absorption of oxygen is estimated and is expressed as a percentage of the amount which would be used by a normal person, taking into consideration the factors of sex, age, height, and weight. In severe hyperthyroidism the B.M.R. may be as much as 170 per cent. of the normal. Such a figure is expressed by the term +70. When the B.M.R. is high the blood cholesterol is usually below normal (170 to 220 mg. per 100 c.c.).

Course of Thyrotoxicosis.—In untreated cases, especially in the younger group of patients, exacerbations tend to alternate with periods of comparative quiescence. In older patients, especially those with auricular fibrillation, the course of the disease may progress steadily downwards, and in the absence of treatment the patient dies of congestive cardiac failure.

Some mild cases may recover completely within twelve months, but as a rule the disease, if left untreated, persists for many years, unless death results from intercurrent infection, heart failure, or exhaustion in a crisis of thyrotoxicosis.

Differential Diagnosis.—Often in acute thyrotoxicosis the diagnosis is obvious at first glance. On the other hand it is sometimes difficult to distinguish between thyrotoxicosis and an anxiety state. In the latter the pulse may be rapid, especially when the patient is first seen, but as a rule it falls to a normal figure when the patient is at rest. With the tachycardia of anxiety sinus arrhythmia is usually well marked, but does not occur in thyrotoxicosis. Patients suffering from anxiety states may exhibit emotional instability not unlike that of thyrotoxicosis.

Occasionally tuberculosis may be suspected when tachycardia and loss of weight are the chief features, but as a rule enlargement of the thyroid or other features help to indicate thyrotoxicosis.

When cardiac symptoms, such as palpitation, dyspnœa, and especially auricular fibrillation are prominent features, it is easy to overlook their thyroid origin. Many cases of hyperthyroidism occur after middle age in patients with adenomata of the thyroid, in which exophthalmos is absent and the symptoms are primarily cardiac. It is therefore *most important always to make a careful examination of the thyroid in every patient who develops obscure cardiac symptoms.*

Treatment.—In mild cases the patient may be kept under observation for some months. Medical treatment in a hospital ward is undesirable, as these patients readily acquire intercurrent infections. In addition the association with disease and death has a bad effect. Sedatives such as phenobarbitone ($\frac{1}{2}$ gr. noct. maneq.) diminish restlessness. Avoidance of domestic worries is important.

Treatment with Thiouracil.—This drug, which is a compound of sulphur and urea, inhibits the utilisation of iodine by the thyroid and thus prevents excessive amounts of thyroid hormone entering the blood stream.

Thiouracil is given by mouth in doses of 0·2 gm. thrice daily (*i.e.*, 0·6 gm. daily). After about ten days of treatment there is a striking improvement in the symptoms, which is accompanied by a fall in the B.M.R. and a gain in weight. The dose is gradually reduced to 0·2 gm. or even to 0·05 gm. daily as a maintenance dose.

Toxic effects occur in 10 to 15 per cent. of cases treated with thiouracil. They may be trivial and transitory, such as drug fever, skin rashes or enlargement of lymph glands, or sufficiently serious to necessitate discontinuing treatment, such as leucopenia of less than 3,000 white cells per cubic millimetre. In order to detect this complication early, white counts should be performed at regular intervals. Agranulocytosis is the most serious danger, for unless dealt with immediately it may be fatal. The patient must therefore be instructed to stop taking the drug at the first appearance of a sore throat or fever, and to report to the doctor, who should at once examine the blood. Fortunately the complication is rare (about 1 per cent. of cases treated) and the mortality is less than $\frac{1}{2}$ per cent.

Many still regard thiouracil as too dangerous for the routine treatment of thyrotoxicosis and advocate its use only in special cases, or pre-operatively. It has been suggested that methyl and propyl thiouracil are less likely to be toxic. If thiouracil or its derivatives are to be used as an alternative to thyroidectomy, the treatment must be persisted in for at least nine months under regular and careful medical supervision. It is possible that in some cases a permanent cure may be effected.

Treatment with Iodine.—The value of iodine in exophthalmic goitre has been thoroughly substantiated. It reduces the B.M.R. to a lower though not to a normal figure and the symptoms of hyperthyroidism become less striking. Iodine medication is mainly useful as a pre-operative measure. If the drug is administered over a prolonged period the initial improvement disappears. Moreover, iodine appears to produce its maximum effect only at its first administration, and a further course of iodine after an interval is of less benefit. It is, therefore, inadvisable to give iodine indiscriminately to patients likely eventually to require operation. It should, however, be given for from ten to fourteen days before operation even in mild cases.

The value of iodine, therefore, lies in the fact that it produces a temporary improvement or remission of symptoms, during which the patient may

safely be submitted to thyroidectomy. It is specially valuable during the "crises" of the disease, in which it rapidly allays the restlessness and excitability, and stops the diarrhœa and vomiting. Thus iodine can render operable many cases that without its use would be too ill to justify operation. As already indicated, similar effects may be obtained with a pre-operative course of thiouracil, though this may increase the vascularity of the gland, and some surgeons employ iodine just before operation to reduce the blood supply.

It is customary to give iodine as Lugol's solution (iodine 5 per cent., potassium iodide 10 per cent.); 5 gr. of potassium iodide daily, however, is equally effective. The temporary exacerbation of hyperthyroidism which often occurs immediately after operation should be combated by large doses of iodine, up to 100 minims of Lugol's solution in the first twenty-four hours. As the patient improves, iodine is withdrawn and may be omitted completely within a week to ten days. If vomiting prevents absorption of iodine by mouth it may be given rectally, or in desperate cases by the intravenous drip injection of sodium iodide (7·5 gr. in a litre of normal saline).

Operative Treatment.—The essentials for success are as follows: (i) A skilful surgeon who has had ample experience of thyroid surgery; (ii) adequate pre-operative treatment; (iii) skilful anæsthesia.

Thyroidectomy is contraindicated in patients whose symptoms are due to an anxiety state, even if there is evidence of some degree of thyrotoxicosis in addition, as the results in such cases are often very disappointing.

It must be realised, however, that even the most successful operation does not cure the patient forthwith, though there is often a striking and rapid improvement. A varying period of rest and quietude is necessary, and occasionally a further operation may be required.

When hyperthyroidism occurs in a patient with an adenomatous goitre —so-called toxic adenoma—operation should be performed at the earliest possible moment. Even with a decompensated heart and auricular fibrillation results are often good, and without operation the patient usually dies of cardiac failure. After operation the heart appears to have remarkable recuperative powers. When fibrillation is present digitalis should be given to slow the ventricular rate. Following thyroidectomy the fibrillation often disappears spontaneously. If this does not occur quinidine should be tried, provided there has been no evidence of congestive cardiac failure (*vide* p. 412).

MYXŒDEMA

Myxœdema is a chronic disease of adults resulting from deficiency of thyroid secretion, characterised by a low basal metabolism, increase of weight, thickening of the skin, and mental disturbance.

The disorder is more common in women than in men and occurs most frequently after the age of forty. Its onset is usually insidious, and may be due to functional exhaustion of the gland as the result of long-continued stimulation. Histologically the normal structure of the gland is replaced by fibrous tissue. Sometimes myxœdema occurs in the late stages of exophthalmic goitre, or it may follow partial thyroidectomy if too much of the thyroid has been removed.

Symptoms.—In myxœdema most of the symptoms are the reverse of those found in hyperthyroidism.

1. *Thyroid Gland.*—This is either normal in size, or it may be so shrunken as to be impalpable.

2. *Heart.*—The pulse is slow but the blood pressure is often raised, and arteriosclerosis may be present. The heart may be grossly enlarged and the electrocardiogram show low voltage excursions with diminution or disappearance of the P and T waves (" myxœdema heart ") (*vide* p. 403).

3. *Weight.*—There is a marked gain in weight, often amounting to over a stone in a few months. This is due partly to the low rate of basal metabolism, partly to the thickening of the skin and subcutaneous tissues.

4. *Nervous System.*—Patients with myxœdema become slow both in physical movements and cerebration. Psychoses with schizophrenic tendencies are not uncommon. They lose their memory and suffer from apathy and somnolence. Special senses are often blunted, especially hearing.

5. *The Skin.*—The changes which occur in the skin and subcutaneous tissues give the myxœdematous patient a characteristic expressionless appearance. A general thickening and infiltration of these tissues occur all over the body ; this differs from ordinary œdema in that there is no pitting on pressure. A muddy yellow complexion with a superimposed mauvish-pink malar flush is characteristic and the finer features become obliterated, so that eventually all patients with myxœdema show a remarkable resemblance to one another. The skin is dry and scaly, and the nails become brittle and atrophic. The hair is coarse, breaks easily, and may become scanty, not only on the head, but all over the body, and especially in the axilla. Loss of hair on the outer sides of the eyebrows is characteristic.

6. *Temperature.*—The temperature is usually subnormal ; myxœdematous patients are particularly sensitive to cold and feel very much better in hot weather.

7. *Alimentary System.*—The appetite is usually poor and constipation is common. Sometimes abdominal distension as a result of deficient peristalsis in the intestines is troublesome.

8. *Basal Metabolic Rate.*—This is always low and may be reduced to 30 or 40 per cent. below normal. As a result of treatment with thyroid extract the rate rises to normal, and at the same time the body temperature increases.

9. *Blood Cholesterol.*—The normal figure is between 170 and 220 mg. per 100 c.c. and in myxœdema it is always raised, usually above 250 mg.

The disease if left untreated is steadily progressive, and death occurs from exhaustion or intercurrent infection. Its duration extends over many years. There is often a moderate degree of hypochromic anæmia, which improves when the patient is treated with thyroid.

Apart from the fully developed condition of myxœdema described above, minor degrees frequently occur in which the patient becomes listless and apathetic, without the development of the characteristic changes in the skin. These forms of the disease, known as hypothyroidism rather than myxœdema, probably result mainly from prolonged overstimulation and consequent exhaustion of the thyroid. It is important, however, to refrain from diagnosing hypothyroidism simply on a history of recent gain in weight.

Treatment.—Fortunately we have in thyroid extract a specific remedy, which is always effective. It is given by mouth as tablets of a dried extract of thyroid (Thyroideum B.P.) in doses of $\frac{1}{2}$ to 4 gr. The initial dose is $\frac{1}{2}$ gr. twice or three times a day, and this must be cautiously increased until the symptoms of myxœdema are relieved. It is seldom that more than 3 gr. a day are necessary. Useful guides as to the quantity required are the temperature, the pulse-rate, and estimation of the B.M.R. Overdosage may cause palpitation and tachycardia. When the correct dose has been found it must be continued indefinitely if relapse is to be avoided.

Cretinism.—This condition is one of hypothyroidism, occurring in infancy. It is specially common in regions where goitre is endemic, and is due to a failure of the thyroid to develop during fœtal life.

At birth the infant may appear normal, but within a year it becomes obvious that its progress, both as regards growth and intelligence, is delayed. Growth, particularly of the extremities, remains stunted, and an adult cretin may retain the stature of a child. The centres of ossification are late in appearing, and the two centres for the carpal bones which are normally present at birth fail to appear during the first year of the cretin's life. Dental development is similarly affected and the teeth are poorly and irregularly formed. The tongue is large and thickened and tends to protrude from the mouth. The skin is rough and dry, the nostrils wide, and the nose sunken. The abdomen is distended, an umbilical hernia is often present, and constipation is marked. The development of the intellectual faculties is always delayed and usually remains permanently below normal, especially if treatment is not commenced at an early age. Diagnosis is aided by an estimation of serum cholesterol, which in the hypothyroid child reaches figures of between 250 and 600 mg. per 100 c.c., whereas the normal for children is 100 to 300 mg.

Treatment is by the administration of thyroid extract. Its effects, especially if started early in life, may be remarkably satisfactory. Dosage varies considerably in individual cases, but is usually about 2 gr. of the dry extract daily, though it is well to start cautiously with daily doses of $\frac{1}{4}$ gr., as hypothyroid children are especially intolerant of overdosage. This must be continued throughout life, which is not necessarily curtailed by the disease.

PARATHYROID GLANDS

The parathyroid glands are four minute bodies embedded in the tissue of the thyroid. Removal produces tetany, which is characterised by increased excitability of the motor nerves with tremors and muscular spasm. The parathyroids may be removed or damaged as a result of partial thyroidectomy, and in such cases tetany may occur shortly after the operation.

The parathyroids secrete a hormone which regulates calcium metabolism. The normal serum calcium figure is about 9 to 11 mg. per 100 c.c.; in tetany, due to parathyroid deficiency, the serum calcium may fall as low as 6 mg. per 100 c.c.; administration of parathyroid hormone raises the serum calcium; prolonged administration mobilises calcium from the bones and thereby increases the amount of calcium in the blood.

Hyperparathyroidism.—This usually results from a parathyroid adenoma. The serum calcium is raised—often to 15 mg.—and the calcium excretion

in the urine is increased. The inorganic phosphorus in the serum is decreased.

The removal of calcium from the bones may give rise to the rare condition of *Generalised Osteitis Fibrosa Cystica*, in which the bones become decalcified and cystic. Spontaneous fractures occur and may render the patient, usually a child, bedridden. More often hyperparathyroidism leads to formation of renal calculi, often bilateral. The possibility of hyperparathyroidism should always be borne in mind when renal calculi are discovered in young adults without urinary infection. In such cases if the serum calcium is raised, exploration of the parathyroids is justifiable.

Tetany

The clinical manifestations of tetany, though characteristic of parathyroid deficiency, occur frequently in other conditions. Tetany is common in infants, particularly in association with rickets and gastro-intestinal disorders (*vide* p. 187). In adults typical attacks of tetany due to alkalosis very occasionally occur in pyloric obstruction (*vide* p. 181). Similar attacks result from pulmonary hyperventilation and are sometimes described as "spontaneous overbreathing tetany." The hyperpnœa is hysterical. Tetany may also occur during pregnancy or lactation and may also follow operations on the thyroid.

Symptoms.—The most prominent symptoms of tetany are the muscular cramps, which affect particularly the extremities. The attacks of cramp last for a variable time, from a few minutes to several hours, and are usually painful. The hands and forearms are most commonly affected, and during a spasm assume a characteristic position. The fingers are flexed at the metacarpophalangeal and extended at the interphalangeal joints; the thumb is adducted into the palm, and the fingers are drawn closely together, thus producing what has been termed the "main d'accoucheur." The wrists and elbows are flexed and the arms adducted. When the condition affects the feet a similar attitude is produced. In severe cases there may be generalised epileptiform convulsions.

Between the attacks there is hyperexcitability of the motor nerves. An attack of tetany may be initiated by pressure around the arm, for instance, by a sphygmomanometer cuff (Trousseau's sign). That the spasm produced is dependent on reflex action rather than local anæmia is proved by the fact that both hands are affected simultaneously. Similarly, tapping the facial nerve close to its point of exit from the stylo-mastoid foramen provokes a spasm of the facial muscles (Chvostek's sign). In infants, laryngospasm is common, particularly in cases of rickets (*vide* p. 188).

Course and Prognosis.—The duration and severity of tetany depend mainly on its cause. In infants the condition usually improves quickly, and is rarely fatal. After thyroidectomy the attacks of tetany may last for many months, but gradually become less severe, possibly owing to regeneration of parathyroid cells.

Treatment.—Infantile tetany is dealt with elsewhere (*vide* p. 187). For tetany in adults, particularly that following operations on the thyroid, parathormone is valuable. This preparation is biologically standardised and must be given hypodermically. The dosage should be controlled by estimations of the serum calcium, which must not be allowed to rise much

above about 10 mg. per 100 c.c. In adults the initial dose required is about 30 units twice a day, and later this may be reduced to 30 units daily. After some weeks or months the symptoms of tetany may pass off even though the serum calcium remains subnormal. This is probably due to the nervous system having become accommodated to the altered state of the blood. Tetany can also be controlled to some extent by administration of calcium, which may be given by mouth as calcium lactate in 10-gr. doses at two-hourly intervals, or as intramuscular injections of calcium gluconate. A milk diet with abundant lactose also helps to prevent tetany. With a meat diet, symptoms are usually aggravated.

ADRENAL GLANDS

Physiology.—The adrenal gland consists of two parts—cortex and medulla—separate, both in development and function. The medulla is derived embryologically from the cells which form the sympathetic nervous system, while the cortex is mesodermal in origin. The cortex plays a part in the regulation of the metabolism of sodium and chloride, and also secretes androgens which influence the development of secondary sex characters both in the male and the female. The medulla secretes adrenaline, which is discharged into the blood stream. This has a specific stimulating effect on sympathetic nerve endings, and its presence in the blood leads to vaso-constriction, a rise of blood pressure, dilatation of the bronchioles, and conversion of glycogen in the liver into glucose. Though the action of adrenaline is very transient it may produce dangerous effects if a large dose is injected rapidly. It is inadvisable to give more than 5 minims of 1 in 1,000 solution without waiting to observe its effect.

Experimental removal of the adrenals or their destruction by disease produces a marked loss of tone in the vascular system and asthenia, which ultimately results in death. The adrenals become exhausted during acute infections and also in severe traumatic injuries and extensive burns. Bilateral adrenal hæmorrhage occurs in the hæmorrhagic forms of the specific fevers, particularly in meningococcal septicæmia (*vide* p. 55).

Addison's Disease

In 1855 Addison published a paper entitled "On the Constitutional and Local Effects of Disease of the Suprarenal Capsules," in which he described as follows the characteristic features of the disease which has come to bear his name: "Anæmia, general languor and debility, remarkable feebleness of the heart's action, irritability of the stomach, and a peculiar change of colour in the skin."

Symptoms.—The cardinal symptoms of Addison's disease are marked and progressive asthenia, low blood pressure, pigmentation of the skin and buccal mucous membranes, and alimentary disturbances. The severity of the symptoms fluctuates, and at times there are exacerbations or "crises" during which the blood pressure falls, vomiting is severe, and collapse is alarming. Death usually supervenes in the absence of effective treatment.

1. *Asthenia.*—Languor, debility, and loss of muscular power are the symptoms which first indicate the onset of the disease, and the patient may be indisposed to undertake work, either physical or mental.

2. *Blood Pressure.*—Both the systolic and diastolic readings are low, and the former rarely exceeds 100 mm. of mercury when the disease is first diagnosed. In the later stages there is a steady fall in blood pressure.

3. *Pigmentation.*—This symptom may be the first sign of the disease. Rarely it is completely absent throughout. There is generalised discoloration of the skin, especially marked in the flexures and the naturally pigmented areas of the body. The colour varies from light brown to black, and the pigment is distributed as small spots or larger areas. In the mouth irregular patches of pigmentation appear on the mucous membrane of the lips and cheeks, upon the gums, or the palate.

4. *Alimentary System.*—There is nearly always a history of loss of appetite, indigestion, " bilious attacks," or vomiting.

Attacks of vertigo and syncope are frequent and are probably due to peripheral circulatory failure. The blood count is usually normal, though sometimes there may be a mild hypochromic anæmia.

In the absence of treatment death is usually not long delayed once the typical symptoms have developed. Occasionally it is the result of an intercurrent infection, but more often it occurs suddenly. Rarely life is prolonged for several years.

Morbid Anatomy.—The characteristic picture of Addison's disease is produced by two pathological conditions only, either bilateral destruction of the glands by a fibro-caseous tuberculous process, or more rarely by an atrophy of the glands, which is sometimes so extreme that no trace of suprarenal can be discovered at autopsy. Active tuberculosis elsewhere is unusual.

Diagnosis.—As with all diseases as rare as Addison's disease, the diagnosis is not infrequently proved to be wrong. Pigmentation, asthenia, loss of appetite, and low blood pressure may be the most prominent features in cachectic states due to carcinoma, anorexia nervosa, and Simmonds' disease. Pigmentation of the buccal mucosa is, however, absent in these conditions. The possibility of pigmentation as the result of descent from non-European ancestors must be borne in mind.

An important feature of the condition is a diminution of the serum sodium, and a figure lower than 315 mg. per 100 c.c. is in favour of the diagnosis. A drop in the blood chlorides is more variable and therefore of less importance. The blood potassium may be raised, particularly during a relapse.[1]

Treatment.—Oral administration of sodium chloride (about 200 gr. daily) is therefore beneficial in maintaining health in the intervals between crises. This treatment should be continued throughout the patient's life. In view

[1] Laboratory tests based on restriction of sodium and provocative administration of potassium, such as the Cutler test, are apt to induce a crisis, and are best avoided. A simple and useful procedure is the Kepler test. It depends on the failure to produce water diuresis in Addison's disease. The volume of urine passed between 10.30 P.M. and 7.30 A.M. is compared with the volume of hourly specimens from 9.30 A.M. to 12.30 P.M., 9 c.c. per pound body weight of water being drunk between 8.30 and 9.30. Should the volume of any one of the morning specimens exceed the night volume, the diagnosis of Addison's disease is unlikely. If, on the other hand, the night volume exceeds the volume of each of the hourly morning specimens, the diagnosis is possible, and it is necessary to proceed to further investigations based on the fact that urea is retained in the blood and chlorides are lost in the urine. For this purpose the following equation has been devised :—

$$A = \frac{\text{urea in urine}}{\text{urea in plasma}} \times \frac{\text{chloride in plasma}}{\text{chloride in urine}} \times \frac{\text{volume of largest hourly specimen of day urine}}{\text{volume of night urine}}.$$

If A equals more than 30 the patient is not suffering from Addison's disease ; if less than 25 he is, provided nephritis is excluded.

of the hypoglycæmia which is often found in Addison's disease the patient should take plenty of glucose.

During the crises of Addison's disease it is necessary to give intravenous glucose saline to restore the serum ionic values and the loss of fluid. Cortical extract should be given in daily doses of 20 to 100 c.c. in the saline.

A synthetic product, desoxycorticosterone acetate, is also available. This substance is marketed as an oily suspension for intramuscular injection under the names of Percorten and Doca and has been shown to exert a very striking beneficial effect in Addison's disease. The usual daily dose is 5 mg., though larger doses are indicated in periods of crisis. Subcutaneous implantation of this hormone (usually 2 to 4 pellets of 100 mg. each) produces a prolonged effect and in conjunction with sodium chloride may maintain the patient in good health for six months to a year, after which another implantation may be performed.

Tumours of the Adrenal Glands

Medullary tumours are rare and arise either from the chromaffin cells (phæochromocytoma) or from the sympathetic ganglion cells (neuroblastoma). The former is accompanied by paroxysmal hypertension. The blood pressure may rise to alarming heights and the patient develops hypertensive encephalopathy (*vide* p. 593). Between paroxysms it may be almost normal. Excision of the tumour may produce permanent cure. Neuroblastoma occurs only in children and is highly malignant.

Cortical tumours give rise to the adreno-genital syndrome of which the chief feature is masculinisation, which differs in severity according to the age at which the tumour appears. It occurs during fœtal life only in females and leads to pseudo-hermaphroditism. Before puberty the condition is most marked in boys, in whom the genitalia develop adult proportions, usually with precocious sexual desire. There is growth of hair, especially on the face, axillæ, and pubis, and there may be excessive muscular development—the so-called infant Hercules type.

In adults the condition is most often seen in women who show signs of virilism, varying from minor degrees of hypertrichosis to a condition closely resembling Cushing's syndrome (*vide* p. 223) with localised obesity, amenorrhœa, masculinisation of the external genitalia, and hypertension. The adreno-genital syndrome may be due to simple hyperplasia of the deepest layer of the cortex, the androgenic zone, or to a cortical adenoma in which malignant changes may subsequently occur. It is associated with greatly increased urinary excretion (over 100 mg. per twenty-four hours) of androgenic substances, measured as 17-ketosteroids. This provides the surest diagnostic sign of an adrenal cortical tumour. Assistance may be obtained by intravenous pyelography in determining in which gland the growth is situated by defining the position of the kidney, which may be displaced downwards if the tumour is large. Treatment of an established tumour, especially when there is evidence of malignancy, is surgical, and consists in the removal of the affected adrenal.

In the milder forms of adrenal virilism characterised only by hirsuties and, possibly, raised blood pressure, so serious a course as surgical interference is unwarranted. In such cases a tumour is seldom present. Unfortunately hormone therapy has so far proved ineffective, and there is no alternative to local remedies for removal of the excessive and unsightly growth of hair.

THYMUS GLAND

Little is known of the physiology of the thymus. Experimental extirpation of the gland has not given constant results. The gland enlarges until puberty, and after that time becomes smaller, until in late middle life practically none of it remains.

The thymus is found to be enlarged in certain diseases, notably exophthalmic goitre, acromegaly, and myasthenia gravis, but perhaps the commonest condition in which thymic hyperplasia is found is "status lymphaticus." This term is employed to describe a condition sometimes found at autopsy in persons who have died suddenly without apparent cause, most often during an anæsthetic. In such cases the thymus is often considerably enlarged, and there is also some general increase in the lymphoid tissue throughout the body. Status lymphaticus is unlikely to be diagnosed during life. When death occurs it results from sudden cessation of the heart beat rather than from respiratory failure.

In infants an enlarged thymus may give rise to paroxysms of dyspnœa, which have been termed thymic asthma. There may be marked stridor and cyanosis, which occasionally result in death.

THE MENOPAUSE

Apart from their reproductive functions the gonads play an important part in the development of secondary sexual characters, and, in the woman, are largely concerned with the regulation of the menstrual cycle. Their secretions are therefore chiefly the concern of the gynæcologist and the endocrinologist. No medical textbook, however, would be complete without an account of the menopause.

This is a normal physiological process of failing ovarian function which usually occurs between the ages of forty-five and fifty-five, though it not infrequently appears much earlier, and in women who have always given a history of menstrual instability it may even develop in the early thirties.

It is associated with a disturbance of the balance of secretion of gonadotropic and ovarian hormones. In some women this phase is symptomless; in others it gives rise to so many and so diverse complaints that it almost merits the name of a disease. Indeed it is perhaps the commonest condition which the practitioner is called upon to treat in women of middle age.

The chief symptoms in order of their frequency are nervousness, hot flushes, excitability, undue tiredness, depression and emotional instability, irritability, insomnia, tachycardia, palpitation and breathlessness, giddiness, lack of concentration and poor memory, headaches, numbness and tingling.

Associated disturbances are atrophic conditions of the vulva and vagina, such as kraurosis and senile vaginitis, hyperkeratosis, scleroderma, pigmentation and papillomata of the skin, hypertension, migraine, arthritis and involutional melancholia.

The most characteristic of the symptoms are the "hot flushes." These may occur many times in the day and awaken the patient at night. They usually last but a few minutes and may come on suddenly and without

apparent cause. A sensation of great heat is experienced and the skin becomes flushed. Perhaps most important of all are the nervous symptoms. The patient is irritable and readily upset by trifles, and makes life a burden not only to herself but to all around her. Obsessions and delusions may occur, and the whole character and outlook may change.

Treatment.—This consists in administration of œstrogens. Of these the cheapest and most effective are the "synthetic œstrogens," such as stilbœstrol, hexœstrol, and dienœstrol. Stilbœstrol is the best known, and probably the most effective, but in a small percentage of cases, and especially when the daily dose is above 1 mg., it gives rise to toxic symptoms such as nausea and headache, and occasionally vomiting. Hexœstrol and dienœstrol are considerably less effective, and probably therefore less toxic. In the case of stilbœstrol it is seldom necessary to give more than 0·5 mg. daily by mouth. The aim should be to give the lowest dose that will control the symptoms and to discontinue treatment as soon as possible. Should the patient show intolerance to synthetic œstrogens, "natural œstrogens" in the form of œstrone should be substituted, of which even such low doses as 3,000 to 6,000 international units daily may prove adequate.

THE PITUITARY GLAND

Physiology.—The pituitary consists of a glandular portion, the anterior lobe and pars intermedia, embryologically derived from the foregut by an upward growth from the naso-pharynx, known as Rathke's pouch, and a nervous element, the posterior lobe, consisting of a downgrowth of neuroglial tissue from the diencephalon.

The anterior lobe is composed of cells, 50 per cent. of which, the chromophobe cells, contain no granules and probably represent the resting phase of the secreting cell. Of the remainder, the chromophil cells, three-quarters contain acid-staining granules, the eosinophil cells, while coarse basophilic granules are found in the rest, the basophil cells. The chromophil cells secrete directly into the vascular sinuses which they surround. At least six endocrine activities have been ascribed to the anterior lobe. These are :—

1. The *growth* hormone, which is secreted by the eosinophil cells and regulates skeletal growth. Up to the present, administration of pituitary extracts to stimulate or accelerate growth in cases of pituitary infantilism or other types of dwarfism has proved disappointing.
2. The *gonadotropic* factors, which control the functional activity of the ovary and testis. Three types of extract are at present available :—

   Chorionic gonadotropin secreted by the placenta and derived from the urine of pregnant women. It is the presence in excess of this factor in pregnancy urine which forms the basis of the Aschheim-Zondek and Friedman tests for pregnancy. Injection of pregnancy urine extracts in the form of Antuitrin-S, Gonan, Physostab, Pregnyl, etc., induces descent in suitably selected cases of undescended testicle.

Serum gonadotropin derived from the blood serum of pregnant mares. This induces follicular maturation and spermatogenesis in infantile animals.

Pituitary gonadotropin derived from the pituitary glands of such animals as oxen, sheep, etc. It is said to contain a synergic factor which enhances the effect of chorionic gonadotropin.

3. The *thyrotropic* hormone, which controls the activity of the thyroid gland.
4. The *lactogenic* hormone, which stimulates the secretion of milk from the mammary glands.
5. The *corticotropic* hormone, which controls the activity of the adrenal cortex.
6. The *diabetogenic* principle, which antagonises the effect of insulin, and the *ketogenic* principle, which facilitates the conversion of fats to liver glycogen with a tendency to the production of ketosis.

The pars intermedia is usually described as belonging to the posterior lobe. It consists of a thin strip of tissue composed of layers of basophil cells, similar in structure to those of the anterior lobe. Its secretions pass by way of the pars nervosa into the cerebrospinal fluid of the third ventricle. It is probable that interference with this path by lesions in the posterior lobe, the pituitary stalk or the overlying hypothalamic region may give rise to disorders of fat, carbohydrate or water metabolism, leading to obesity, lowered sugar tolerance, or diabetes insipidus. The pars intermedia secretes two hormones. One of these, *vasopressin*, stimulates smooth muscle, producing constriction of the capillaries, peristalsis of the intestines, and contraction of the muscle surrounding the mammary ducts, resulting in the expression of previously secreted milk—galactogogue effect. It also inhibits the flow of urine. The other, *oxytocin*, stimulates uterine contractions. Commercial extracts of the posterior lobe, such as " pituitrin," contain both the factors, which are also separately available under such trade names as " pitressin " (vasopressin) and " pitocin " (oxytocin).

Adenomata of the Pituitary

The commonest tumour of the pituitary is an adenomatous proliferation of cells of the anterior lobe. Such adenomata may be chromophobe, eosinophil, or basophil.

1. **Chromophobe Adenoma.**—Since the chromophobe cells produce no endocrine secretion the only disturbances resulting from a chromophobe adenoma are due to pressure on neighbouring structures. The remaining cells of the anterior lobe may be compressed, as indicated by the development of such symptoms as amenorrhœa or impotence. The tumour may encroach upon the boundaries of the sella turcica, showing radiographic evidence of generalised enlargement of the pituitary fossa or erosion of the posterior clinoid processes. It may enlarge upwards and burst through the diaphragma sellæ and involve the overlying structures. Thus the fibres of the optic nerves which carry impulses from the nasal halves of the retinæ and cross in the optic chiasma may atrophy from pressure and lead to bitemporal hemianopia (*vide* p. 580). Signs of increased intracranial pressure may

develop, and an attempt should then be made to remove the growth. Other suprasellar tumours which may give rise to similar "neighbourhood" symptoms are tumours of the pituitary stalk and cysts of Rathke's cleft, and tumours arising in embryonic rests of Rathke's pouch, which are known as cranio-pharyngiomata.

2. **Eosinophil Adenoma.**—When the tumour develops before the epiphyses have fused, there is a generalised skeletal overgrowth with the production of *gigantism*. There is seldom a proportionate increase of muscular strength, and the pituitary giant is generally clumsy, feeble, and readily fatigued. Development of the adenoma in adult life leads to the condition of *acromegaly*. The onset is usually insidious. Thickening of the soft tissues is as much responsible as actual changes in the carpal and tarsal bones and phalanges for the characteristic enlargement of the extremities. The fingers become clubbed and the hands increase in breadth, giving them a spade-like appearance. The gradual changes in the facial appearance finally render the patient unrecognisable to any friend who has not seen him since the onset of the disease. The malar bones, the nose, and the lower jaw become unduly prominent. The teeth become spaced and the lips and tongue are coarsely thickened. The voice becomes rough and deep owing to thickening of the vocal cords and enlargement of the larynx. There is a generalised enlargement of all the viscera—splanchnomegaly. The appetite may be excessive and constipation a troublesome symptom. Thirst and polyuria are sometimes observed. Commonly there is a lowered carbohydrate tolerance with transient glycosuria. Usually the sexual functions are ultimately depressed with amenorrhœa and virilism in the female and impotence and loss of libido in the male. Should the tumour increase greatly in size, the pituitary fossa enlarges and "neighbourhood" symptoms appear. Surgery may be indicated if these become severe. Some success has been achieved by deep X-ray therapy, particularly in relieving headaches and the constriction of the visual fields. The disease usually runs a prolonged course and the symptoms are seldom incapacitating, though the change in appearance may be distressing.

Basophil Adenoma (*Cushing's Syndrome*).—Unlike other types of pituitary adenoma, this tumour is usually small and intrasellar and does not give rise to pressure symptoms. It most commonly occurs in young adults or in early middle age. It affects women three times as often as men. The syndrome is characterised by both metabolic and endocrine disturbances. The appetite may be ravenous and there is excessive thirst and polyuria. Sugar tolerance is lowered with hyperglycæmia and glycosuria in some cases. Obesity of the face, neck, and trunk, especially of the lower abdomen, is striking and may develop rapidly. Abdominal striæ appear, but, unlike those which follow pregnancy or rapid increase in weight, they are purple in colour and are less likely to fade. Extensive ecchymoses may be seen on the arms and legs, and spectacular bruises result from trivial injuries. Fractures of the long bones occur from insufficient cause, and frequently osteoporosis of the upper thoracic vertebræ gives rise to kyphosis. The blood pressure is raised, often to very high levels, *e.g.*, 250 systolic and 160 diastolic. The patient may develop any of the severe symptoms seen in malignant hypertension (*vide* p. 430), such as severe headache, visual disturbances due to hypertensive retinopathy (*vide* p. 509), and attacks of cardiac asthma. The patient presents a plethoric appearance with

polycythæmia. Men suffer from impotence. In women there is amenorrhœa with virilism, hirsuties, acne, and acrocyanosis.

The syndrome may be difficult to distinguish clinically from adrenal virilism, though the 17-ketosteroid value in the latter condition is much increased, whereas in Cushing's syndrome it is usually normal. In every case that has come to autopsy there has been some evidence of increased adrenal cortical activity, and in many an adrenal tumour has been found. In some cases there has actually been no evidence of a pituitary adenoma, but in these cases, as in all the others, a characteristic hyaline degeneration of basophil cells has been found. Treatment is disappointing and transient in its effect. It consists in efforts to check the excessive activity of the basophil cells either by courses of deep X-ray therapy to the pituitary gland or by administration of large doses of œstrogens or androgens. Surgical removal of the gland has been attempted in a few cases, but it is an heroic procedure which, if successful, sometimes leads to symptoms of pituitary deficiency such as are seen in Simmonds' disease. Prognosis is not invariably grave and in many cases the condition appears to be self-limiting.

Pituitary Insufficiency

1. Simmonds' Disease.—This condition develops as the result of a destructive lesion of the pituitary gland, always involving the anterior lobe and sometimes affecting the posterior lobe as well. It occurs far more frequently in women than in men, and often follows pregnancy or abortion, particularly when associated with a post-partum hæmorrhage. It is due to loss of the stimulating influence of the pituitary on all the other endocrine glands, especially the gonads, thyroid, and adrenals. The most striking symptom, when it is present, is extreme general emaciation ("pituitary cachexia"). It does not necessarily occur, however, and many cases have been described in which the loss of weight has been insignificant. The teeth and hair rapidly fall out, and one of the striking features of the clinical picture is the complete absence of axillary and pubic hair. There is loss of sex desire associated with impotence in the male and amenorrhœa in the female. The basal metabolic rate is usually very low, readings of −60 having been recorded. The temperature is subnormal and the patient is sensitive to cold. The skin becomes smooth and pale. The blood pressure is always low and muscular weakness is usually marked. The blood sugar is low and sugar tolerance is increased. Constipation is the rule, and attacks of abdominal pain and vomiting have been described. Diagnosis is often difficult, and the condition may be mistaken for Addison's disease, myxœdema, or anorexia nervosa. Though there may be many features of adrenal cortical failure, pigmentation is never present and indeed the skin is characteristically white. The basal metabolic rate is usually even lower than in the most advanced case of myxœdema, and although the skin is dry it never shows the typical myxœdematous deposits. In anorexia nervosa the patient is restless and full of energy, and apart from the loss of weight, often in remarkably good health. The loss of pubic and axillary hair is a useful diagnostic sign in Simmonds' disease, and indeed mild hirsuties is commonly seen in anorexia nervosa. The diagnosis should be confirmed by estimation of the 17-ketosteroids, which are either absent or very low. In anorexia nervosa they are normal, though in myxœdema they may show

a low value. An insulin tolerance test, however, shows a slow return to the basal blood sugar level in Simmonds' disease, whereas in myxœdema it may show an abnormally low value at first but returns to the basal figure at the end of two hours.

Treatment with every available anterior pituitary extract is usually disappointing. Methyl testosterone given by mouth in daily doses of 30 mg., or implantation of testosterone is, however, a surprisingly effective method of substitution therapy. Thyroid should be used cautiously. High doses have been known to precipitate attacks similar to Addisonian crises.

2. **Pituitary Infantilism.**—This condition, which occurs during childhood, is seldom fatal, and little opportunity has been afforded for examination of the pituitary after death. There is a general retardation of skeletal and bodily growth, and the patients remain dwarfed but not deformed. The sexual functions may also fail to develop. There is no mental retardation, nor do the patients become obese, as is the case in Fröhlich's syndrome. The facial appearance may later become prematurely old and the skin wrinkled. Treatment with the growth hormone preparations at present available is disappointing.

Disorders related to the Pituitary and Hypothalamus

There is a group of conditions usually described as being due to pituitary deficiency in which the lesion may lie anywhere on the path between the pituitary and the third ventricle, *i.e.*, in the anterior or posterior pituitary, in the stalk, in the hypothalamus, or in the nucleus supra-opticus. The following disorders belong to this group :—

1. **Pituitary Obesity.**—This condition affects the female more frequently than the male, especially in adult life. Indeed it is striking how much more sensitive the pituitary-hypothalamic pathway is to external influences in the case of women. Adult men seldom suffer from " functional " pituitary disorders. The obesity may follow pregnancy, emotional shock, or environmental disturbance. It may be rapidly progressive and is of a characteristic distribution, involving the abdomen (the " pituitary apron "), the hips and thighs, the upper arms from the outer surfaces of which almost localised lipomata develop, as they do also in the popliteal fossæ. The breasts may become pendulous and enormous. A characteristic feature is fluid retention. Treatment is disappointing, though rigid diet may be, at least temporarily, effective. Thyroid extract in doses commencing at $1\frac{1}{2}$ gr. daily and rising by $\frac{1}{2}$ gr. daily each fortnight until the resting pulse-rate exceeds 90 may also be helpful. In a small percentage of cases diuretics such as mersalyl given in doses of 1 or 2 c.c. twice weekly by injection, possibly in combination with ammonium chloride (*vide* p. 418), reduces the weight considerably, if only temporarily. Complete starvation enhances the diuretic effect of mersalyl, and 4 or 5 lbs. may be lost in a day with this combination. If carried out in hospital this treatment may lead to the loss of $1\frac{1}{2}$ to 2 stones in a fortnight.

2. **Fröhlich's Syndrome.**—The onset of the disease commonly occurs between the ages of eight and ten, and is comparatively sudden, being marked by a rapid increase in weight which is often accompanied by a cessation or slowing of skeletal growth. The disease may or may not be due to a pituitary tumour or to a lesion on the hypothalamic-pituitary

pathway, and X-ray evidence of an enlarged pituitary fossa or calcification of a cranio-pharyngioma may be found. In those cases which are not due to an organic lesion of the pituitary, and which are therefore not strictly cases of Fröhlich's syndrome, spontaneous improvement may occur after puberty, and it is possible that they represent a comparative functional failure of the pituitary at a time of life when normally a great strain is placed upon it.

In the male child the penis is small and the testes remain undeveloped and may be undescended. The fat is largely deposited around the pelvic girdle, the upper part of the thighs, the lower abdomen, and the breasts, giving the patient the general appearance of a female rather than of a male. A marked degree of knock-knee results from the mechanical effects of overweight. Diminished sugar tolerance is often also found. Diabetes insipidus is occasionally an associated condition. Often the subjects of the disease are intellectually bright and do well at school.

The outlook in cases of Fröhlich's syndrome will naturally depend on whether a tumour is present. If this is so, "neighbourhood" symptoms may develop and require relief by operation. When the disease is due simply to pituitary hypoplasia or hypothalamic involvement the patient may live for years, but owing to the obesity is prone to die from intercurrent infections.

As regards treatment, strict diet is most likely to be effective, though sometimes thyroid extract is also found to be useful. There is too frequent a tendency to attach the diagnosis of Fröhlich's syndrome to fat children whose obesity is simply due to overeating and lack of exercise, and it should be borne in mind that the essential triad of symptoms in Fröhlich's syndrome are retardation of skeletal and sexual development, and obesity. In any case two or three months' dietetic restriction is an excellent prelude to any subsequent treatment. If a tumour of the pituitary is the cause of the symptoms, a radical operation or a decompression may have to be attempted.

3. **Diabetes Insipidus.**—In this condition the main symptoms are polyuria, thirst, and emaciation. The amount of urine is enormously increased, and may be as much as 20 pints in the twenty-four hours : it is of extremely low specific gravity and free from both albumin and sugar. The patient is much inconvenienced by frequency of micturition both by day and night, and naturally very large quantities of fluid have to be taken in order to avoid dehydration.

Occasionally the disease has been found to occur in families, presumably as the result of a hereditary factor. It has also been known to follow head injuries.

The condition may last for many years without fatal effects, and treatment by extract of the posterior lobe is usually effective. Subcutaneous injections of pituitrin produce a marked diminution in diuresis, which lasts for six to twelve hours. It is usually necessary for the patient to have two injections a day of $\frac{1}{2}$ to 1 c.c. of the extract, although if pitressin tannate is used the effect of the injection is prolonged, sometimes for as much as forty-eight hours. Administration of adequate doses of the hormone or the tannate may produce unpleasant symptoms due to intense peripheral vasoconstriction and intestinal peristalsis. Unfortunately oral administration, either of the extract or of the dried glands, is completely without effect. A dried powder of the posterior lobe may be used as a snuff and is effectively

absorbed. This form of treatment has the advantage that smaller doses may be given at more frequent intervals. The dose most commonly employed is 10 mg. three times a day.

Polyuria in diabetes insipidus is due to a failure of the epithelium of the renal tubules to reabsorb chlorides and water. Restriction of chloride intake is therefore indicated.

In diabetes mellitus polyuria is associated with glycosuria. Chronic interstitial nephritis may produce marked polyuria and frequency, but albuminuria, a raised blood pressure, and cardiac hypertrophy will decide the diagnosis. In hysteria, polyuria occurs, but is purely transient.

P. M. F. Bishop.
J. J. Conybeare.

DISEASES OF METABOLISM

DIABETES MELLITUS

THE amount of glucose in the blood remains remarkably constant in healthy persons, and is expressed either in milligrammes per 100 c.c. of blood or in grammes per cent. When fasting, the total reducing bodies in the blood, both arterial and venous, mainly consisting of glucose, are between 80 and 120 mg. per 100 c.c. (0·080 to 0·120 per cent.). Even an hour after large amounts of carbohydrate it rarely rises above 170 mg. and is usually less, and within two hours it has fallen to the fasting level. Chemical methods which estimate only the glucose and not other reducing bodies give figures about 20 mg. per 100 c.c. lower. In this book the term blood sugar will be employed in its generally accepted sense as indicating the total reducing bodies in the blood.

The relative stability of the blood sugar is effected by the interaction of many factors, which may be considered separately.

1. *The Pancreas.*—The internal secretion of this organ produced by the *islets of Langerhans* and known as insulin is the most important factor in the regulation of the blood sugar. There is a steady and continuous production of insulin by the healthy pancreas, and in addition its output is increased when food, particularly carbohydrate, is taken. The exact mode of action of insulin is incompletely understood, but it probably renders the glucose in the blood available for storage as glycogen in the liver and the muscles. Thus if the output of insulin is insufficient the blood sugar is increased, and when it reaches a level of approximately 170 mg. per 100 c.c. sugar passes through the kidneys and is excreted in the urine. This level of blood sugar is usually described as the *renal threshold.* When the blood sugar is below the renal threshold the urine contains no sugar, when it is above it glycosuria is present. The importance of the renal threshold is discussed later in connection with renal glycosuria.

2. *Liver.*—This organ is the main site both for the formation and storage of glycogen and its conversion to glucose. If the liver is removed in an experimental animal the blood sugar rapidly falls to very low figures and the animal dies in hypoglycæmic convulsions. If adequate glucose is injected intravenously the blood sugar rises and the animal recovers rapidly. This experimental work on hepatectomised dogs first gave the clue to the elucidation of the symptoms of hypoglycæmia in man (*vide* 239). In clinical practice hypoglycæmia as a result of liver dysfunction is almost unknown, as the extent of damage to the organ has to involve practically the whole liver.

3. *Pituitary Body.*—The hormones produced by the pituitary, especially those of the anterior lobe, oppose the action of insulin and raise the level of blood sugar. Although hyperactivity of the pituitary through its diabetogenic hormone may raise the blood sugar and produce glycosuria, it is unlikely that this gland plays an important part in diabetes mellitus.

4. *Adrenals.*—The internal secretion of the adrenal medulla (adrenaline) stimulates the conversion of glycogen in the liver into glucose, hence the value

of adrenaline in the treatment of hypoglycæmia (*vide* p. 240). The hormone secreted by the adrenal cortex opposes the action of insulin and under certain circumstances may produce hyperglycæmia. The part played by the adrenals in the ætiology of diabetes is probably small.

5. *Thyroid.*—Excess of thyroxin aggravates the severity of diabetes, and a diminution of thyroid activity lowers to some extent the level of blood sugar.

Pathogenesis of Diabetes.—Although, as has been shown above, the liver and endocrine glands probably play a part in the control of the blood sugar, the most important factor in the development of diabetes is the pancreas. Thus the experimental ablation of that organ produces the disease. Additional proof is the fact that insulin, the internal secretion of the pancreas, can rectify the metabolic anomalies of diabetes. It is true that there are no constant post-mortem findings in the pancreas of diabetics. The reserve of the healthy pancreas, like that of other vital organs, such as the liver and kidneys, is very great, and probably at least seven-eighths of the gland must be destroyed before diabetes develops. It is not surprising, therefore, that growths of the pancreas or even more widespread lesions, such as acute pancreatitis, rarely produce diabetes. Hæmochromatosis is the only disease of the pancreas which almost invariably produces diabetes.

It is probable that diabetes more often results from one or both of the following factors : (i) an inherent insufficiency in the islet tissue or insular reserve ; (ii) disturbances of metabolism which make additional demands on the islet cells. The first factor, inherent insufficiency in the insular reserve, is often inherited and probably accounts for the frequency of familial and racial diabetes. The main disturbance of metabolism which produces diabetes is obesity. The majority of diabetics who develop the disease in middle or later life have been much overweight ; this throws an extra strain on all the organs, including the pancreas. Less often hyperthyroidism, especially if long-continued, may produce diabetes.

Although the metabolic disturbance in diabetes mellitus primarily involves carbohydrate metabolism, the disease, at any rate in its more severe forms, if untreated, interferes with the metabolism of fat and protein in addition. The abnormal breakdown of fats produces an excess of ketone bodies, β-oxybutyric acid, aceto-acetic acid (diacetic acid), and acetone. Their accumulation in the blood gives rise to the clinical picture of ketosis and diabetic coma (*vide* p. 242), and they are also excreted in the urine and through the lungs. In severe diabetes, untreated with insulin, the patient may excrete far more sugar than the amount of carbohydrate taken in the food, and this excess is produced by the conversion into glucose of protein and to a less degree of fat. If insulin and carbohydrate are given, ketosis is abolished.

Symptoms and Diagnosis of Diabetes Mellitus.—In mild diabetes, symptoms may be completely absent for years, although glycosuria may be continuously present. In more severe cases thirst, polyuria, and loss of weight are prominent features. The irritation by the glucose in the urine often causes balanitis or pruritus of the vulva. With severe diabetes and ketosis the tongue becomes dry, red, and painful, and there may be general dehydration of the tissues. The urine contains glucose, often up to 5 per cent., and ketone bodies may also be present. Although it is true to say that all untreated diabetics pass sugar it cannot be assumed that the finding of glucose in the urine necessarily indicates diabetes. Actually this is very far from the truth, and many patients have been subjected to unnecessary hardship by the

unwarranted diagnosis of diabetes on the strength of glycosuria alone. Diabetes can be diagnosed with certainty when typical symptoms such as polyuria, thirst, and wasting are present in conjunction with glycosuria. When the only grossly abnormal finding is glycosuria a full investigation is essential. The point at issue can be settled with certainty by the *blood-sugar tolerance* curve.

Before carrying out this investigation the patient should have been taking a normal mixed diet for some days without restriction of carbohydrate. Having eaten no breakfast he empties his bladder and has a blood-sugar estimation done. This gives the fasting blood-sugar level. He then takes 50 gm. of glucose dissolved in approximately 100 c.c. of iced water flavoured with lemon. Further blood sugars are done at half-hourly intervals for two and a half hours. A normal person will have a fasting blood sugar ranging from 80 to 120 mg. per 100 c.c., while that in a diabetic will tend to be considerably higher. In fact a fasting blood sugar of over 130 mg. is presumptive evidence of diabetes.

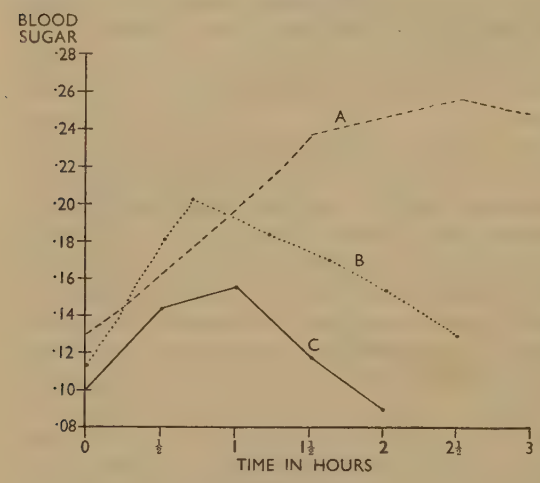


FIG. 8

A, Curve from severe diabetic. B, Curve from mild diabetic. C, Normal curve.

Diabetic and normal blood sugar tolerance curves are shown in Fig. 8. It will be noted that in the normal person though the blood sugar may rise to 160 mg., or even over, in the first hour after the ingestion of glucose, it falls rapidly and within one and a half to two hours it is down to or below the fasting level. A diabetic, however, behaves very differently. The rise of blood sugar is very prolonged and at the end of two hours it has quite failed to approximate to the fasting level, and, at any rate, in diabetes of moderate severity, it may remain very high for hours. While the blood sugar is above the normal renal threshold or "leak-point," which is usually about 170 mg., sugar is present in the urine.

In so-called *renal glycosuria* glucose passes through the kidneys at blood-sugar levels well below the normal leak-point. In such cases, although sugar may be more or less constantly present in the urine, the blood-sugar curve is perfectly normal. Renal glycosuria produces no symptoms and calls for no treatment.

A further group of cases has been described by Maclean under the term "lag curve." An example of this is given in Fig. 9. It will be observed that the blood sugar rises rapidly to a point much in excess of the normal, but the fall to normal is equally abrupt and is complete within two hours. Sugar is passed in the urine during the period when the blood-sugar level is above the normal renal leak-point. Maclean suggested that there is a delay or "lag" in the action of the sugar storage mechanism, but the rapid rise in blood sugar is more probably due to rapid absorption from the intestine in persons whose stomachs empty unusually fast. Glycosuria of the "lag curve" type

is not uncommon following gastro-jejunostomy. None of the symptoms of diabetes are present, and there does not appear to be any special liability to develop the disease. Occasional urine examinations and blood-sugar estimations should be carried out in order that early warning of any change in the type of glycosuria may not be overlooked.

Transient glycosuria is not uncommon in healthy persons as the result of excitement, such as a life insurance examination. Cannon and Fiske found that out of twenty-five members of the Harvard University football team no fewer than twelve had glycosuria after the Harvard *versus* Yale match. That excitement and not exertion was responsible is proved by the fact that five out of the twelve who had glycosuria were acting as reserves and did not actually take part in the game. Such glycosuria is purely temporary and is due to stimulation of the suprarenals. The urines of the Guy's Hospital Rugby football team passed immediately after the Hospital Cup Final showed no glycosuria, though all contained albumin except that of the full-back. Possibly football in Great Britain is less productive of emotional excitement than in the United States. A head injury or generalised convulsions, such as epilepsy, may lead to similar transient glycosuria.

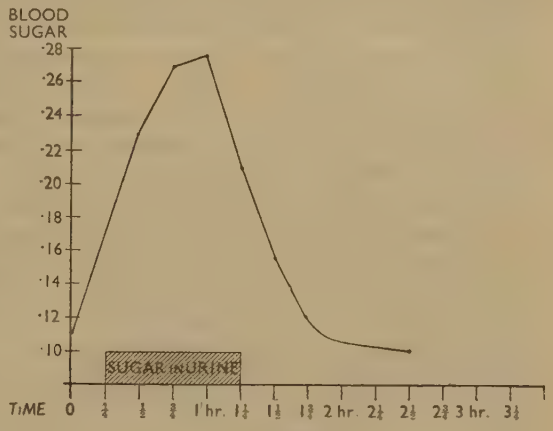


Fig. 9
"Lag curve."

Examination of Urine for Sugar and Ketones.—This is of such paramount practical importance that the details of the tests are summarised briefly below :—

1. *Fehling's Test.*—Equal amounts of freshly prepared Fehling's solution and urine are boiled in separate test tubes and while boiling are mixed. The mixture is brought back to boiling point momentarily. If sugar is present the liquid becomes turbid and the colour changes to green or red. Fehling's solution is reduced to some extent in a concentrated urine by creatinine or uric acid.

2. *Benedict's Test.*—Eight drops of the urine are run into a clean test tube and 5 c.c. (one teaspoonful) of Benedict's qualitative solution added. The mixture is then boiled for two minutes. If sugar is present the solution becomes turbid and changes colour to green, yellow, or red according to the quantity of sugar present. The fact that the reducing body is glucose can be proved by the preparation of an osazone or by fermentation tests with yeast.

Tests for Ketone Bodies.—From the point of view of treatment the presence of ketones is even more important than is that of sugar.

1. *Rothera's Test.*—About 10 c.c. of urine are saturated with crystals of ammonium sulphate, and a few drops of a freshly prepared solution of sodium nitroprusside added. The solution is then made alkaline with strong ammonia. A purple colour develops if ketones are present.

2. *Gerhardt's Test.*—About 10 c.c. of the urine are placed in a test tube and a 10 per cent. solution of ferric chloride is added drop by drop. A white

precipitate of phosphate forms and redissolves, and if diacetic acid is present the colour of the solution becomes red.

Rothera's test is very delicate, and unless the purple colour is deep and develops rapidly it does not necessarily indicate a dangerous ketosis. A strongly positive Gerhardt test, on the other hand, is a danger signal. If the patient has been taking aspirin or salicylates, the urine becomes purple or violet in colour with ferric chloride, which may obscure the red colour due to ketones. The Rothera test is unaffected by these drugs.

Complications of Diabetes.—These are numerous and important. In fact, since the advent of insulin diabetic complications are more potent factors in morbidity and even in mortality than the diabetes itself. Diabetic coma is dealt with elsewhere (*vide* p. 242).

1. *Boils and Carbuncles.*—These are relatively common, especially in mild untreated diabetes. In all such cases the urine should be tested for sugar. Large carbuncles are always especially dangerous in diabetics.

2. *Peripheral Neuritis.*—This is described on page 700.

3. *Gangrene.*—Elderly diabetics are specially prone to develop gangrene of the toes or feet. This serious complication is very rare before the age of fifty. Diabetic gangrene is always associated with atheroma of the vessels, but this is liable to occur at an abnormally early age in diabetics.

There are two factors which lead to gangrene in diabetics : (i) impairment of the blood supply owing to arteriosclerosis ; (ii) diminished resistance of diabetic tissues to trauma and infection. The extent to which the circulatory factor is operative may be judged from the presence or absence of pulsation in the dorsalis pedis and posterior tibial arteries. Pain is often very severe and the gangrene may be moist or dry.

The decision as to whether amputation is necessary is often a very difficult one. If the gangrene is spreading rapidly, and no arterial pulsation can be felt, immediate amputation is required. When, however, there is much infection of the tissues, and particularly when undrained pus is present, more conservative surgical measures are justifiable in conjunction with chemotherapy. It is frequently found that healing may take place in a few months, particularly if the diabetes is controlled with insulin. Persistent and severe pain associated with gangrene is an indication for early amputation.

4. *Pulmonary Tuberculosis* (*vide* p. 244).

5. *Ocular Complications.*—Cataract is common in elderly diabetics, as is diabetic retinitis, especially in arteriosclerotic patients.

6. *Xanthochromia and Xanthoma Diabeticorum.*—Xanthochromia is a yellowish discoloration of the skin, especially on the face and palms of the hands. It is due to carotene and lipochrome pigments. Its occasional appearance in diabetics is probably due to large amounts of vegetables in the diet.

In xanthoma diabeticorum numerous bright yellow tumours appear on the skin. There is usually a high blood cholesterol. The condition is chiefly seen in severe diabetics.

Types of Diabetes and Prognosis.—Diabetes may appear in every grade of severity from a symptomless glycosuria to a fulminating type of the disease in which coma is the first symptom. Speaking generally the younger the patient the more severe and acute the diabetes, though this is by no means invariably true. On the whole familial and hereditary diabetes tends to be mild or moderate in severity. The great majority of diabetics can be main-

tained in perfect health and vigour by insulin. Needless to say, except in its mildest forms, the prognosis of the disease depends mainly on the patient. Consistent disregard of either diet or insulin will lead to serious deterioration or even death. Diabetes in children is described on page 241, and the effects of pregnancy on page 245.

Diabetes in elderly persons is usually benign in its course and seldom calls for more than qualitative dietetic restrictions. Gangrene is, however, a dangerous complication.

TREATMENT OF DIABETES

In the treatment of diabetes, either with or without insulin, four general principles must be fulfilled.

1. The patient must be given a diet which is adequate in caloric value to enable him to carry on a useful and active life and yet avoid over-nutrition. Though occasional glycosuria is inevitable, the passing of large quantities of sugar must be prevented.

2. The diet must be so balanced in regard to content of protein, carbohydrate, and fat that he does not develop ketosis.

3. The diet must be so arranged that it conforms as closely as possible with that of normal individuals.[1]

4. If treated with insulin the dosage must be regulated to avoid so far as is possible both hyperglycæmia and insulin reactions (*vide* p. 239).

As regards the first of these principles, it is obvious that the caloric requirements of individuals must vary widely, depending on their age, sex, size, and occupation. Infants and children require diets of a relatively high caloric value to allow for growth as well as for the normal metabolic requirements (*vide* p. 241). With increasing age caloric requirements decrease. Persons engaged in heavy manual work require larger diets than those in sedentary occupations. The terms " basal " and " maintenance " diets are often used. A " basal " diet is one which will provide an adequate number of calories for a person at complete rest ; a " maintenance " diet is one containing sufficient calories for an ordinary active life. From a practical point of view, however, the " maintenance " diet is of chief importance, as the diabetic must be able to lead a life of unrestricted activity. For adult patients it is generally sufficient to allow 35 to 40 calories to each kilo of body weight (16 to 18 calories per pound of body weight). Thus between the ages of twenty and fifty the following figures may be regarded as adequate for an ordinary life calling for no heavy manual work :—

Weight.	Caloric Requirements.
10 stones	2,500
11 ,,	2,800
12 ,,	3,100

For female patients about 10 per cent. of the calories may be deducted. The caloric requirements of children are discussed elsewhere (*vide* p. 241).

Needless to say, the nutritional state of the patient will have an important

[1] Rationing has increased difficulties of diet for diabetics, even though extra rations of meat, butter, and cheese can be obtained by application through the Local Food Office. Patients are advised to join the Diabetic Association, 152 Harley Street, London, W.1. The Association publishes a journal of great value to diabetics.

bearing on the caloric content of the diet. If the patient is emaciated, the diet must be relatively high, whereas in a diabetic already much overweight a lower diet is advisable. As a check upon the caloric value of the diet a careful record of the patient's weight should be kept from week to week. A steady and continued increase in weight, except in emaciated persons, is most undesirable, while a steady loss of weight indicates in most cases that the diet is too low.

The second general principle is that the patient should be given a diet on which he does not develop ketosis. Fortunately with the aid of insulin it is now possible to allow every diabetic sufficient carbohydrate, in relation to the quantity of fat in the diet, to prevent the formation of ketone bodies.

The amount of protein in the diet must be adequate to replace the constant breakdown of tissue protein. This should be, in adults, about 1 gm. of protein to each kilo of body weight. Probably no harm is done if this is increased slightly, especially in those leading active and energetic lives, but it should rarely exceed 100 gm. High protein diets tend to render stabilisation with insulin difficult. With children and adolescents proportionately larger amounts of protein are required to allow for growth (*vide* p. 241).

The carbohydrate content of the diet necessarily varies with the age and sex of the patient, but for an adult who is leading a normal active life not less than 180 gm. should be allowed, and it is probably preferable in most cases to give up to 230 gm. As much as this can rarely be taken even in mild diabetes except with insulin (*vide* p. 237). The amount of fat depends on the caloric requirements, but high fat diets with a relatively low carbohydrate content are both unpalatable, expensive, and tend to produce ketosis.

The third general principle in the construction of a diabetic diet is that it should conform as closely as possible to the type of diet eaten by healthy persons. This not only saves expense and trouble in the household, but it enables a diabetic to play his part in social life and prevents the development of an inferiority complex. Special diabetic foods should never be necessary.

Bearing in mind what has been said above, we may now proceed to consider the treatment of patients suffering from diabetes. However obvious the diagnosis may be, it is most important to make a *thorough physical examination, including an X-ray of the chest*, before the institution of treatment. This may reveal the presence of other pathological conditions such as tuberculosis, arteriosclerosis and heart disease, cholecystitis or gall-stones, focal sepsis in teeth or tonsils, all of which have a bearing on the treatment of the diabetes.

Needless to say, the line of treatment to be adopted in individual cases will vary with the severity of the disease. The first question which usually needs decision is whether the patient should start on insulin at once, or whether dietetic treatment alone should be tried to begin with. There are five indications for starting insulin immediately: (i) coma or incipient coma, (ii) the presence of considerable ketosis as indicated by a positive Gerhardt test or a strongly positive Rothera test, (iii) complications such as phthisis or the necessity for a surgical operation, (iv) emaciation, where the patient obviously requires a high caloric diet, (v) the presence of complications of diabetes, such as retinitis, impaired circulation in the feet, and neuritis. If none of the above conditions are present, it is often justifiable—except in infants and children—to test the patient's reaction to undernutrition diets. Starvation is never necessary, as it not only submits the patient to unnecessary

hardship but it also often produces ketosis, as the patient during starvation is really living mainly on his own body fat. Below are given two test diets containing respectively approximately 1,100 and 1,450 calories. In both of these the fat is sufficiently restricted to inhibit ketosis. The patient should be first of all placed on No. 1 diet, and its effects noted on the excretion of sugar over a period of five to seven days. If on this relatively low diet, sugar does not either disappear or become very greatly diminished, it is obvious that insulin will be required. During the period of the test, specimens of urine should be obtained four times a day and the results carefully recorded on a chart such as that on page 236. Such a chart enables the progress of the case to be seen at a glance.

If on diet No. 1 the patient becomes sugar-free he may be put on to No. 2, and later, provided he remains sugar-free, the diet may be built up with further gradual additions of carbohydrate and fat until an adequate maintenance diet is reached. It is important that the carbohydrate in the diet should be more or less evenly distributed throughout the day.

DIABETIC TEST DIETS

APPROXIMATE FOOD CONTENT

No. 1		No. 2	
Protein	65 gm.	Protein	75 gm.
Carbohydrate	90 ,,	Carbohydrate	140 ,,
Fat	50 ,,	Fat	65 ,,
Calories	1,100 ,,	Calories	1,450 ,,

Breakfast

1 egg or small kipper.
Tomatoes.
2 oz. milk.
1½ oz. bread.
⅓ oz. butter or margarine.

Lunch

2 oz. lean meat or fish.
2 oz. potatoes.
Green vegetables (5 per cent. group).
1 small orange or apple.

Supper

Clear soup.
2 oz. lean meat or fish.
2 oz. potatoes.
Green vegetables (5 per cent. group).
1 oz. cheese.
1½ oz. bread.
Coffee (black) or tea.

Breakfast

1 oz. breakfast cereal, or 1 oz. oatmeal for porridge.
7 oz. milk.
1 egg or small kipper.
2 oz. bread.
⅓ oz. butter.

Lunch

2 oz. lean meat or fish.
Green vegetables (5 per cent. group).
2 oz. bread.
½ oz. cheese.
⅓ oz. butter.

Dinner

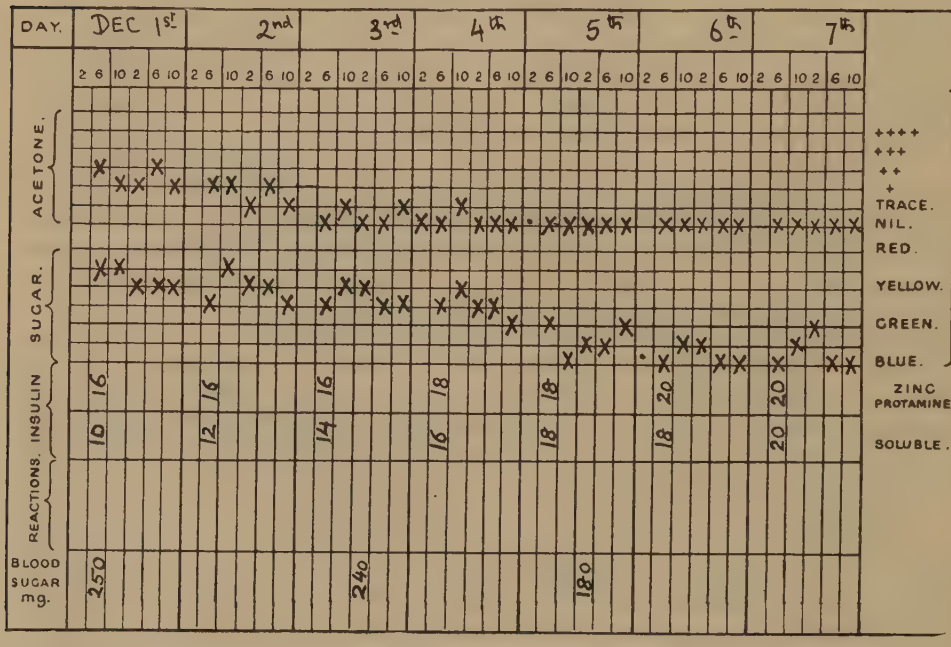
Clear soup.
3 oz. lean meat or fish.
Green vegetables (5 per cent. group).
4 oz. potatoes.
⅓ oz. butter.
4 oz. milk.
1 orange or apple.
Coffee or tea.

NOTES.—The vegetables and fruits in the 5 per cent. group (*vide* p. 241) may be taken as desired, as their food value is low. All other food should be carefully weighed, until the patient has become experienced in estimating weight. Clear

soup, tea, and coffee have no food value and may be taken as desired. No alcoholic beverages and no special diabetic foods may be taken without the doctor's permission. When fish is taken instead of meat ½ oz. of butter may be added.

Quite apart from the dietetic treatment of diabetes, careful attention must be paid to the general health of the patient, particularly as regards focal sepsis. In the presence of an infection, insulin, both endogenous and exogenous, works inefficiently. The teeth should be X-rayed and any which may be septic removed. If the tonsils show signs of chronic infection, tonsillectomy should be performed. Elderly diabetics should pay particular attention to the feet; these should be washed daily, carefully dried, and sprinkled with boracic powder. Shoes must be large and not rub the toes. Neglect of these precautions increases the liability to gangrene. The bowels should be kept open regularly. Mental worry and anxiety must be avoided. Although it is never justifiable to promise a cure, it may be pointed out that diabetics who adhere carefully to the instructions given to them may live a practically normal and useful life for an indefinite period.

DIABETIC CHART.



Insulin Treatment.—Insulin is now available commercially in three forms, (i) soluble insulin (S.I.), which is an acid solution of insulin hydrochloride with a maximum action within two to four hours after injection; (ii) zinc protamine insulin (Z.P.I.), an alkaline suspension which acts much more slowly (*vide* p. 238); (iii) globin insulin, which is intermediate in its action between soluble and zinc protamine insulin (*vide* p. 239). Insulin is standardised in units by its effect in lowering the blood sugar in rabbits. Soluble insulin is supplied commercially in three strengths, 20, 40, and 80 units in each cubic centimetre. These strengths are often described as

" single," " double," and " quadruple." As a rule with doses up to about 12 units, " single " strength insulin is used and with larger doses one or other of the more concentrated varieties. Z.P.I. and globin insulin are supplied in double or quadruple strengths.

If insulin treatment is deemed necessary a decision has to be made as to whether S.I. or Z.P.I. is to be used. The latter is advisable, at any rate as an initial measure in stabilisation, only in patients with relatively mild diabetes and no ketosis. When symptoms such as thirst, polyuria, and loss of weight are prominent it is safer to initiate treatment with S.I. When stabilisation has been effected it is often possible to change to Z.P.I. or a combination of both.

The patient is first put on a diet containing approximately 150 gm. of carbohydrate, with 1 gm. per kilo of protein and enough fat to bring the calories to about 1,800 per diem. Stabilisation can be effected more rapidly and efficaciously in hospital than in the home, but there is rarely any necessity for treatment in bed. A careful urine chart should be kept. If soluble insulin is used the initial dose should be 10 units in the morning and 5 units in the evening. The amount of insulin can be increased by 5 units daily. Thus on the second day of treatment it would be 10 units morning and evening, on the third day 15 units and 10 units. In more severe cases, especially if the urine contains much sugar and ketones are also present, the initial doses may be larger, *e.g.*, 20 or more units each. The insulin should be given half an hour before the morning and evening meals. In a few cases it may be necessary to give insulin before the midday meal in addition to the morning and evening doses.

Increases in insulin dosage are controlled mainly by the urinary findings. When sugar disappears or is present in very small amounts the insulin should be increased more gradually. Hypoglycæmic reactions (*vide* p. 239) are an indication to reduce the insulin or to increase the carbohydrate intake. Blood-sugar estimations should be made when the urinary sugar has much decreased or disappeared. The blood should be taken before the morning or the evening injections, as the readings at these times are likely to be at their maximum.

When the patient has been stabilised on this diet, further increases must be made in order to raise it to a maintenance level. Sometimes no additional insulin is required, but if glycosuria recurs the amount of insulin should be gradually increased. When soluble insulin is being given it is advisable that the bulk of the carbohydrate should be taken in the meals following the injections of insulin.

Opinions differ considerably as to the amount of carbohydrate which should be included. There is general agreement that a very low carbohydrate ration (*e.g.*, 70 gm. *per diem*) is undesirable, as it renders the patient specially liable to ketosis, and is also unpalatable. Moreover, on a low carbohydrate diet patients feel less fit and less energetic than when larger amounts are allowed. Rabinovitch and others advocate extremely large amounts of carbohydrate, even up to 300 gm. a day. On such a diet the amount of fat has to be restricted very severely, or the patient will be found to be taking an over-nutrition diet. Probably it is best to give between 180 and 250 gm. of carbohydrate daily. This allows an adequate amount of fat to be included. Diabetics doing heavy manual work will of course need a diet containing more carbohydrate and a high calorie content.

Rationing has inevitably led many diabetics to increase their carbohydrate intake very considerably. Many indeed are taking a practically normal diet. There is no evidence that this change in dietetic regime has had any deleterious effects, such as an increased liability to diabetic coma or other complications, so long as sufficient insulin is administered. It is possible that the restrictions on diet imposed in the past for insulin cases were unnecessarily severe.

When an uncontrolled diabetic is brought under the influence of insulin there is often a sudden deterioration in vision, which may render reading difficult. This is due to refractive changes in the lens resulting from changes in the water balance of the body. The vision rapidly returns, though new glasses may be necessary.

Occasionally allergic reactions develop at the site of injection forming red and indurated areas, which are sometimes tender, These usually cease to occur after a few days. If they do not, a change of the brand of insulin to one made from a different animal, *e.g.*, pig, may be effective.

Zinc Protamine Insulin.—As a result of work by Hagedorn and Scott, an insulin has been produced, the action of which is more prolonged than is the case with ordinary insulin. Whereas the latter controls the blood sugar for only about four to five hours, the new product—usually known as Z.P.I.—has a far longer duration of action, probably up to twenty-four hours if 40 units or more are given daily. Moreover, owing to slow absorption it is less precipitate in its action.

Diabetics of only moderate severity, particularly those over forty years of age, can usually be controlled by a single morning injection of Z.P.I., but severe diabetics may need both kinds of insulin, soluble to control glycosuria after breakfast and protamine zinc to control the diabetes during the later part of the day and during the night. Soluble insulin and Z.P.I. are best injected separately, using two syringes. The same needle may be used if the injection site is altered by moving the needle under the skin.

Z.P.I. is liable to produce severe hypoglycæmic reactions which sometimes come on insidiously, so that the patient may have no initial warning symptoms. Consequently it is important that the dose of Z.P.I. should be increased gradually, and patients who are being stabilised on this insulin should be under close medical observation.

Patients undergoing stabilisation with Z.P.I. should take not less than 150 gm. of carbohydrate a day. This should be spread evenly throughout the main meals and a small carbohydrate feed at bedtime is required. For a patient who has not had insulin previously, an initial morning dose of 12 to 24 units, according to the severity of the diabetes, is advisable, and the dose can be increased by 6 units every third morning until absence of glycosuria or low blood-sugar readings indicate that the dose is sufficient. When a patient who has previously been taking two doses a day of S.I. desires to change over to Z.P.I., the best plan is to give him his ordinary morning dose of S.I. and in addition three-quarters of the number of units of Z.P.I. as he has been accustomed to take of S.I. in the evening. The dose of S.I. is then gradually cut down and that of Z.P.I. increased until stabilisation has been effected. As has been stated above, it is often necessary to give both types of insulin indefinitely.

The advantages of zinc protamine insulin are that in most diabetics of moderate severity a single daily injection replaces two injections of soluble insulin, and its slower absorption diminishes the fluctuations in blood sugar

which sometimes occur in patients taking soluble insulin. It is rarely possible to stabilise a diabetic on Z.P.I. alone if he needs more than 40 units. In such cases, S.I. will be needed in addition to Z.P.I. in order to control glycosuria during the morning.

Globin Insulin.—This is intermediate in its action between S.I. and Z.P.I. Its effect on the blood sugar begins soon after injection, reaches its maximum after about eight hours, and thereafter gradually subsides to disappear in about twenty hours. In some cases it may be more effective than S.I. in controlling glycosuria in conjunction with Z.P.I.

Hypoglycæmic Reactions.—When insulin lowers the blood sugar below about 65 mg. per 100 c.c., characteristic symptoms are produced, which are usually termed hypoglycæmic or insulin reactions. The blood-sugar level at which these occur varies considerably in different patients. The initial symptoms of a reaction are tremor, sweating, and a sensation of hunger, or a sinking feeling in the epigastrium. When the blood sugar falls there is probably increased activity of the suprarenals in an attempt to mobilise glucose from the tissues. This may readily produce the above symptoms as side effects. The patient also may become confused, agitated, noisy, hilarious or quarrelsome. Sometimes acute alcoholism is closely simulated. In more advanced hypoglycæmia there may be twitchings, paralyses, convulsions, and coma. Reactions are most likely to occur two to four hours after an injection of soluble insulin, but sometimes they may be delayed for eight hours or more.

The factors which are likely to produce reactions in a patient taking insulin are as follows :—

1. Errors in measuring the dose or the inadvertent use of double or quadruple strength insulin.
2. Increase in carbohydrate tolerance after stabilisation.
3. After recovery from infections or sepsis, both of which conditions produce a temporary decrease of carbohydrate tolerance.
4. Delay or omission of a meal after an injection of insulin.
5. Gastro-intestinal disturbances which interfere with the absorption of carbohydrate.
6. Unaccustomed physical exercise, especially if prolonged. This is probably due to depletion of the stores of glycogen in the liver.

Hypoglycæmia due to Z.P.I. sometimes gives little warning of its onset owing to the gradual but prolonged fall in the blood-sugar level. It is likely to occur in the evening or during the night. The prodromal symptoms of sweating and tremor are often absent, and continued headache and malaise may be prominent features. It reacts to treatment less readily than that due to soluble insulin, and even when consciousness has been regained, relapse into coma is not uncommon, unless the administration of glucose is continued.

Hypoglycæmia following either S.I. or Z.P.I. is rarely confused with diabetic coma and the differential diagnosis is discussed elsewhere (*vide* p. 243). Treatment is simple if the patient realises the significance of the symptoms in the early stages. Every diabetic taking insulin should carry with him a few lumps of sugar as an insurance against emergencies. One or two lumps, preferably taken with a little water, will rapidly cut short a reaction. In more severe cases where the patient is unconscious, 10 to 20 gm. of glucose should be given intravenously, or a stomach tube may be passed and 50 gm.

of sugar dissolved in a few ounces of water introduced. Hypodermic injection of adrenaline (10 minims of 1 in 1,000), repeated if necessary, will usually restore consciousness sufficiently to enable sugar to be taken by mouth.

In rare instances *spontaneous hypoglycæmia* has been recorded in patients with a carcinoma or adenoma of the islets of Langerhans in the pancreas, which produces an excess of endogenous insulin. The symptoms are similar to those of reactions due to exogenous insulin, but become progressively more severe and intractable. The condition has been cured by surgical removal of a pancreatic adenoma.

The occurrence of hypoglycæmic reactions in a patient undergoing stabilisation on insulin usually indicates that the dose of insulin is too high. Rather smaller doses should be given, but insulin should not be completely omitted. Special caution should be exercised to avoid reactions in elderly patients. This is most important in patients with a degenerated heart muscle, as a severe reaction may cause anginal attacks or even sudden death. Young children and very emaciated diabetics are specially prone to hypoglycæmia, and in them increase in insulin dosage should be very carefully graduated. In such cases if facilities are readily available for blood-sugar estimations, these are helpful in enabling the medical attendant to gauge the effect of insulin.

Glycosuria and Hypoglycæmia.—Although the ideal to be aimed at in the treatment of diabetes is a normal blood sugar and absence of glycosuria throughout day and night, this ideal can rarely be attained completely in any diabetic who needs insulin without the risk of hypoglycæmia. There is little evidence that at any rate transient rises in the blood sugar above the renal threshold are harmful, and it is certainly better that sugar should be passed in the urine than that the patient should be subjected to the discomforts, risks, or even dangers of hypoglycæmia. Even without the development of definite hypoglycæmic symptoms many patients find that they feel tired and generally unfit if an attempt is made to keep them continuously free from glycosuria. Increase of the carbohydrate ration may abolish reactions without cutting down the insulin. It is of course essential to prevent ketosis.

Education of the Diabetic Patient.—If a diabetic patient is to be treated satisfactorily, it is essential to obtain his intelligent co-operation, or at any rate that of his relatives. In order to adhere to his diet the patient must learn the elements of dietetics, and it is equally important that he should become adept at testing his urine, and giving himself insulin. The wide recognition of the necessity for the education of diabetic patients has led to the publication of many diabetic manuals both in this country and in America, one of which the patient should be made to study as soon as treatment is commenced.

From the beginning of treatment the patient should be taught to test his urine, using Benedict's test. He should give his own insulin injections from the beginning of treatment. He should be warned to avoid repeated injections into the same area of skin, as this may produce localised atrophy, known as *insulin fat atrophy*. As regards diet, all foods except the 5 per cent. vegetable group should be weighed until the patient learns to judge the size of a given portion with reasonable accuracy. In order to avoid monotony in diet the patient must have a knowledge of the content of various foods in common use as regards protein, carbohydrate, and fat in order that he may be able to vary his diet.

All vegetables and fruits contain carbohydrate and they are classified as follows, according to the percentage of carbohydrate present in their fresh state. Tinned vegetables have approximately the same carbohydrate content, but tinned fruits must be forbidden owing to the syrup in which they are preserved.

5 *per cent. vegetables and fruits :* grape fruit, cabbage, lettuce, cucumbers, spinach, asparagus, marrow, celery, tomatoes, watercress, leeks, Brussels sprouts, cauliflower, mushrooms, rhubarb, scarlet runners, French beans.

10 *per cent. vegetables and fruits :* oranges, strawberries, black currants, gooseberries, blackberries, pumpkins, turnips, beets, carrots, onions.

15 *per cent. vegetables and fruits :* plums, apricots, apples, pears, cherries, raspberries, green peas, artichokes, parsnips.

20 *per cent. vegetables and fruits :* bananas, prunes, potatoes, haricot beans, boiled rice, boiled macaroni.

Other sources of carbohydrate are (i) oatmeal, which contains about 66 per cent. of carbohydrate when weighed dry, (ii) bread, which, whether white or brown, contains approximately 50 per cent. of carbohydrate, (iii) milk.

The 5 per cent. group of green vegetables and fruits contains so little utilisable carbohydrate that they may be taken in unrestricted amount even by severe diabetics. All other groups must be taken only in such amounts that the total carbohydrate ration is not exceeded.

Quite apart from the regulation of the amount of carbohydrate in the diet, it is important that the total caloric value shall not be increased by too large amounts of protein and fat. If these are taken in excess, not only will the patient become obese but he is likely to develop ketosis.

The consumption of alcohol in anything except very moderate amounts should be forbidden as diabetics readily develop alcoholic neuritis. Sweet wines and liqueurs should be avoided completely, but spirits, dry wines, and ordinary beer are relatively innocuous.

In calculating the caloric value of foodstuffs it is essential to know that for practical purposes 4 calories are produced by 1 gm. of protein or carbohydrate and 9 calories by 1 gm. of fat. A table is given on the following page showing the food content of some of the common foodstuffs. For more detailed dietetic tables, manuals on diabetes should be consulted.

Diabetes in Infants and Children.—Before the discovery of insulin diabetic children rarely survived more than a few years. With insulin they now grow up normal in stature, physique, and intellect.

The diabetic infant or child has to make good not only the wastage in its tissues but allowance must also be made for the fact that it has got to grow. Consequently more liberal diets, especially as regards protein, are necessary than in the case of adults. Under six years, 3 to 4 gm. of protein must be given per kilo of body weight ; from seven to twelve years, 2 to 3 gm. per kilo ; and between twelve and adult life, 2 gm.

The total calories of the diet must be relatively far higher than in the case of adults, and range from 100 calories per kilo in early infancy to about 50 at age twelve.

Children are more liable to develop ketosis than are adults, particularly when they develop any infection. Consequently a relatively large carbohydrate ration should be allowed. This should be about 100 gm. at age five,

130 gm. at ten, and 180 gm. or more at fifteen. With these amounts of carbohydrates there is little risk of ketosis.

Protein, Carbohydrate, and Fat Contents of Common Foodstuffs

N. B.—The figures given apply to foods as served at table unless otherwise indicated.

1 oz. (=30 gm.) contains—	Protein.	Carbohydrate.	Fat.	Calories (approximate).
	Gm.	Gm.	Gm.	
Vegetables (5 per cent. group)	½	1	0	6
Vegetables (10 per cent. group)	½	2	0	10
Potatoes	1	6	0	30
Oatmeal (dry weight, uncooked)	5	20	2	120
Bread	3	16	0	80
Animal Foods—				
Beef (roast, average)	7	0	9	120
Bacon (fried)	5	0	15	155
Fish—				
Cod (boiled)	6	0	0	25
Herring (fresh, cooked)	7	0	3	55
Dairy Products, etc.—				
Eggs (one, average size)	6	0	6	75
Milk	1	1½	1	20
Cream (average)	1	1	6	60
Cheese (Cheddar)	8	0	10	120
Butter or margarine	0	0	25	225

Infections such as the specific fevers, tonsillitis, or even colds should be treated seriously as they reduce carbohydrate tolerance. The patient should be kept in bed, take plenty of fluids with an ample supply of carbohydrate, and if necessary take increased doses of insulin. Neglected infections predispose to coma, or may produce a permanent decrease in carbohydrate tolerance.

Children are more prone than are adults to develop hypoglycæmic reactions, which are often induced by increased activity and physical exertion. The symptoms are often psychical and the child may be thought to be merely naughty or perverse. More severe reactions with convulsions have sometimes been mistaken for epilepsy.

Insulin is almost invariably necessary in diabetic children. In infancy it is best given at least three or perhaps four times daily, but when the child is of school age, if possible the number of injections should be reduced to two.

Diabetic Coma and its Treatment.—Before insulin, diabetic coma was the most frequent cause of death in youthful diabetics. Insulin has greatly reduced its frequency and diminished its dangers.

The symptoms of diabetic coma are due to the accumulation of acetoacetic acid and possibly other ketone bodies in the blood. When coma is impending, ketone bodies are found in the urine, and the Gerhardt test is strongly positive. In addition, owing to the diminished alkali reserve, the CO_2 combining power of the blood is diminished to 20 volumes per cent. or less.

In diabetic coma the ketone bodies are excreted not only in the urine but through the lungs, and a smell of acetone can often be detected in the breath. Rarely the urine may contain no ketones, though acetone may be present in the breath. In such cases there is a failure on the part of the kidneys to excrete the ketone bodies, which is sometimes due to an associated nephritis.

Occasionally in diabetes of very acute type coma may be the first symptom, but in many cases the condition supervenes in diabetics who are suffering from an acute infection such as a local cellulitis, a general infection such as influenza, or even tonsillitis. In all infections, insulin, whether endogenous, *i.e.*, secreted by the patient's own pancreas, or exogenous, acts less efficiently than normally. The omission of insulin or dietetic indiscretions in a severe diabetic may also precipitate coma.

At the onset of coma, constipation, abdominal pain and vomiting are common symptoms. The appetite fails and the amount of urine is often diminished owing to dehydration of the tissues. The pulse becomes thin and rapid, the blood pressure falls, and the intra-ocular tension is low. The condition is one of peripheral circulatory failure (*vide* p. 419) analogous to surgical shock. The patient becomes first confused and dazed, and if untreated, lapses into a coma from which he cannot be roused. The respirations are deep and sighing, and the term " air-hunger " is often applied to the condition. Without insulin death usually occurs within a few days.

Treatment of Diabetic Coma.—This is quite as urgent a matter as that of an acute abdomen, but before starting active treatment with insulin it is essential that the diagnosis should be verified, especially when coma occurs in patients who are taking insulin. If hypoglycæmia is mistaken for diabetic coma the results are likely to be disastrous. Fortunately there is seldom any real difficulty in the differential diagnosis of the two conditions. The important points are given in tabular form below :—

	Diabetic Coma.	Hypoglycæmia.
Type of onset . .	Gradual (several days).	Very sudden.
Symptoms and signs .	Indigestion, nausea, vomiting, abdominal pain, constipation. Air-hunger and deep respiration. Rapid and thin pulse. Ocular tension low. Skin dry. No convulsions. Acetone in breath.	Sensation of hunger. Shallow respiration. Normal pulse. Ocular tension normal. Profuse sweating. Tremor ; convulsions in late stages.
Urine . . .	Sugar.[1] Ketones. Albumin and casts common.	Absent or trace. Ketones absent. No albumin or casts.
Blood . . .	Glucose usually above 350 mg. per 100 c.c. Urea often raised.	Glucose usually below 60 mg. per 100 c.c. Urea normal.

The essential points in the treatment of coma are given below :—

1. *Insulin.*—This must be given at the earliest possible moment, either subcutaneously or intravenously. The latter route should be adopted in

[1] The presence of sugar in the urine does not necessarily preclude a diagnosis of hypoglycæmia as the urine may have been secreted some hours previously and retained in the bladder.

dangerously ill patients with failing circulation. The insulin in such a case should be given in a pint of saline to which glucose (see below) has been added. The dose will vary with the degree of coma. If the patient is completely unconscious, between 100 and 200 units should be given during the first three hours of treatment, an injection being given hourly. Protamine zinc insulin should not be used owing to its slow rate of absorption.

2. *Glucose.*—During the first few hours of treatment, ½ gm. of glucose should be given for every unit of insulin injected. The object of giving glucose is to abolish ketosis and to prevent unexpected hypoglycæmia. In comatose patients glucose is best administered by stomach tube after washing out the stomach. A Ryle's tube is readily swallowed even by a comatose patient if the bulb of the tube is pushed well to the back of the pharynx. It can be left in position for the later administration of fluids.

3. *Dehydration.*—Patients in coma are always dehydrated. This is best combated in patients with circulatory failure by intravenous drip saline. In comatose patients 2 to 3 pints should be given early in treatment. If there is depletion of sodium chloride, as shown by the absence of chlorides in the urine, hypertonic saline (2 to 3 per cent.) is preferable to normal saline. Fluid may also be given direct into the stomach, but it is important not to give more than about 5 oz. each hour, since large quantities may induce vomiting or even acute dilatation of the stomach. Rectal saline may also be given.

4. *Constipation.*—If the patient is severely ill enemata and purgatives should be avoided until improvement has occurred.

5. *Circulatory Failure.*—The patient must be kept warm and nikethamide (Coramine) be given hypodermically. In desperately ill cases suprarenal cortical hormone (*e.g.*, 10 c.c. of eucortone) may be given intravenously. After recovery, he should be kept in bed for a week.

6. *Infection and Sepsis.*—Coma is frequently induced by infection and sepsis. A careful physical examination should be made and if there is any collection of undrained pus, it should be dealt with surgically at the earliest possible moment.

Patients in diabetic coma should be under continuous medical observation, as the condition may change from hour to hour. Urine should be obtained, by catheterisation if necessary, every three hours, and if the results of blood-sugar estimations are readily available, these are helpful in deciding on the subsequent dosage of insulin. The response of the patient as judged by his clinical condition is of great importance. If there are no signs of return of consciousness further doses of insulin as large as those given initially may be required. The total amount of insulin given during the first twenty-four hours of treatment varies from about 150 to 500 units. When in doubt it is safer to err on the side of too much rather than too little insulin. For several days after coma the diet should consist mainly of carbohydrates ; fat should be reduced to a minimum.

Tuberculosis in Diabetics.—While insulin does not appear to have appreciably decreased the incidence of tuberculosis among diabetics, it has certainly improved what used to be a very grave prognosis. Unfortunately incipient phthisis is rarely diagnosed in diabetic patients, as its early symptoms are often attributed to the diabetes. Every diabetic should have his chest X-rayed as a routine. Deterioration in a diabetic should always arouse a suspicion of tuberculous infection.

A diabetic with phthisis should always take insulin and should be kept on

a high caloric diet. The carbohydrate should be well over 200 gm. daily, and an ample supply of milk is advisable, as well as cod-liver oil.

Pregnancy and Diabetes.—Before the discovery of insulin, pregnancy was rare except in very mild diabetes, and in most severe cases amenorrhœa was constantly present. With effective insulin treatment pregnancy has become not uncommon.

Most pregnant diabetics show a definite loss of carbohydrate tolerance, especially from the sixth month until delivery. This usually necessitates an increase in insulin, which may be as much as 50 per cent. Fœtal death is very common during the later months of pregnancy unless the diabetes is well controlled. Pregnancy produces an increased liability to ketosis, and therefore a relatively high carbohydrate diet is required. The carbohydrate should be not less than 200 gm. *per diem* and the protein allowance should be at least $1\frac{1}{2}$ gm. per kilo of body weight. The blood sugar should not be allowed to exceed 0·16 per cent. Termination of pregnancy is now very rarely necessary.

It must be realised that the presence of a reducing substance in the urine of a pregnant woman does not necessarily indicate that she is suffering from diabetes. Osazones should always be prepared to exclude the possibility of lactose in the urine during the later stages of pregnancy. Also a blood-sugar tolerance curve is called for in cases where the patient is not obviously diabetic. During pregnancy a low renal threshold for glucose is not at all uncommon and considerable amounts of sugar may be passed, even though the blood sugar is within normal limits. Restriction of diet in such cases does nothing but harm. Glycosuria during pregnancy should be thoroughly investigated, as a mild or potential diabetic may develop obvious symptoms for the first time during a pregnancy.

Operations on Diabetics.—With the aid of insulin, surgical operations on diabetics have become possible, which in pre-insulin days would have proved inevitably fatal. No diabetic, however mild, should undergo an operation without being put on insulin. If the operation is not an urgency, the patient should be stabilised on insulin and a diet containing about 200 gm. of carbohydrate with a low fat content. For the twenty-four hours immediately preceding operation he should take orange juice with glucose, oatmeal gruel, and beef-tea. Three hours before operation he should take orange juice with 50 gm. of glucose, which should be administered half an hour after 25 units of insulin.

If the operation is an urgent one, it should not be delayed owing to the diabetes for more than a few hours. If the patient is already taking insulin, his usual dose should be doubled and given at the earliest possible moment. If he is taking zinc protamine insulin, this should be discontinued temporarily and soluble insulin substituted. Glucose should be given by mouth or rectum. A further specimen of urine should be obtained, if possible, after two hours, and if this contains sugar and ketones, further insulin should be injected. It is not necessary, indeed it is usually impossible, to abolish glycosuria, but the control of ketosis is most important. After operation glucose should be given in intravenous saline until fluids can be taken by mouth. If possible 100 gm. of glucose should be taken daily for some days following operation. Insulin should be given in small but frequently repeated doses, the actual amount to be determined on the results of frequent urine and blood-sugar examinations.

Local or spinal anæsthesia should be employed if possible, but if a general anæsthetic is necessary, gas and oxygen is to be preferred. Ether is less

satisfactory owing to liability to post-operative vomiting, and chloroform should never be used.

ACIDOSIS AND ALKALOSIS

Acidosis is said to be present when there is a diminution in the alkali reserve in the blood. It cannot be regarded as a disease in itself and it may arise under many varying conditions. In children there is often an acidosis in cyclical vomiting, but there is no evidence that acidosis is the cause of the condition. Acidosis also occurs in starvation or severe and protracted vomiting. It also may be present in diabetes and nephritis.

Since acidosis is practically always associated with, and dependent on, some other pathological condition, the symptoms present in a patient with acidosis are mainly dependent on the underlying disease. In severe acidosis the most characteristic feature is the deep respiration, often termed "air-hunger." This perhaps depends on the action of the acid on the respiratory centre. Acidosis is often accompanied by headache, nausea, and vomiting.

Acidosis can be prevented by giving adequate amounts of carbohydrate and restricting the amount of fat in the diet. The administration of glucose and sodium bicarbonate will often relieve symptoms of acidosis.

Alkalosis implies an increase in the alkali reserve in the blood. It is an uncommon condition but sometimes arises from the ingestion of large amounts of alkali, such as may occur in the intensive alkaline treatment of peptic ulcer or of nephritis. When there is severe vomiting in pyloric stenosis, alkalosis may follow the loss of acid in the vomit. When alkalosis is considerable the blood urea may be much elevated and the patient may also show signs of tetany.

The chief symptoms of alkalosis are headache, irritability, nausea, vomiting, anorexia, and drowsiness. If the condition is due to the taking of alkaline medicines, these must be discontinued at once, and plenty of fluids given by mouth or rectum. If it is due to pyloric stenosis, operation is required (*vide* p. 308).

GOUT

Gout is a disease characterised by the deposition of sodium biurate in the joints, an increase in the amount of uric acid in the blood, and a tendency to the development of nephritis.

Ætiology.—Referring to gout, Sydenham, himself a sufferer from the disease, wrote, "More wise men than fools are victims of the affection." Although at the present time gout is considerably less common than it was a century ago, the disease is certainly more frequent in private than in hospital practice.

Many factors such as climate, heredity and over-indulgence in food and drink have been regarded as of importance in the ætiology of gout. Of these, perhaps the most important is heredity. Probably 50 per cent. of the cases have a gouty family history. Gout in women is excessively rare. Alcohol has always been regarded as a most important factor in the production of the disease, but it would appear that fermented liquors, such as beer and wines, are more deleterious than are distilled spirits such as whisky or gin. Perhaps an even more important predisposing factor than alcohol is persistent over-

eating. In all probability the frequent occurrence of gout among the English upper classes in the eighteenth century was due to the large meals and liberal indulgence in port which were so characteristic of that period.

Gout is uncommon before forty, and such cases as occur at an earlier age are nearly always inherited.

Pathology.—Although the most striking symptom in gout is an arthritis associated with the deposition of sodium biurate in the cartilages of the joints and in the periarticular tissues, the disease is more than an arthritis and must be classified under the heading of metabolic disorders.

All cell nuclei contain nucleic acid, which is combined with protein. It is from this that the uric acid of the urine is derived. Normally about 1 gm. of uric acid is excreted daily in the urine, and this is derived from two sources : the nucleic acid molecule in the food and that derived from the breakdown of cell nuclei in the body. The former is known as the *exogenous* and the latter as the *endogenous* uric acid. On a purin-free diet endogenous uric acid is alone excreted, but the amount varies in each individual, ranging from 0·5 to 0·7 gm. a day. When purin-containing food, such as liver, kidney, or pancreas, is eaten, only about 25 to 50 per cent. of the purin appears in the urine as uric acid ; the balance is probably destroyed in the blood.

Normally, the blood contains about 2 to 3·5 mg. of uric acid per 100 c.c., which circulates in the form of sodium biurate. In patients with gout there is an increased percentage of uric acid in the blood, and even when foods containing purin are avoided the blood uric acid amounts to between 4 and 7 mg. per 100 c.c., or approximately two to three times that in normal blood. The output of endogenous uric acid in gouty patients is usually low. For a few days before an attack of gout the uric acid excretion falls, but after the development of symptoms a rise in the excretion takes place, with a diminution in the uric acid in the blood. From these facts it would appear that in gout there is a retention of uric acid by the kidneys, but whether the symptoms of gout are solely due to such a retention is more doubtful, as it has been clearly proved that in other diseases, such as nephritis and leukæmia, there is often a considerably greater excess of uric acid in the blood than is the case in gout, yet in those diseases with high blood uric acid no symptoms of gout occur.

Morbid Anatomy.—Gout in itself is not a fatal disease, but death often takes place as a result of associated conditions such as arteriosclerosis with cerebral hæmorrhage, or chronic nephritis with uræmia. A gouty joint examined at autopsy shows, in the cartilage, patches and streaks of a white chalky material consisting of sodium biurate ; this is also found in the periarticular tissues such as ligaments, tendons, and synovial membranes ; in severe and chronic cases the deposition of sodium biurate may infiltrate the skin, which eventually ulcerates, leaving the chalky material exposed ; the ends of the bones in the neighbourhood of joints affected by chronic gout show areas of absorption, translucent in an X-ray plate, where the bony tissue has been replaced by sodium biurate. The joints most commonly affected are the metatarso-phalangeal joints of the big toes, the joints of the fingers, the ankles, knees, and wrists. In addition to the deposits of sodium biurate in the joints, a similar condition is found in the cartilage of the ear ; these deposits are very small and are known as *tophi*.

Symptoms.— *Acute Gout.*—The clinical picture of an attack of acute gout is so characteristic that the disease in this stage is seldom misdiagnosed.

The patient as a rule has been in good health, and is awakened during the night by acute pain in one of the big toes. The pain is excruciating, and there is a burning sensation, as if a hot iron was being pushed into the toe-joint; pressure or movement aggravate the pain. With the approach of morning the symptoms abate somewhat, but the joint is red and glazed in appearance, slightly swollen and very tender. The temperature is usually raised and there is anorexia and malaise. The pain recurs on successive nights and the joint becomes more markedly swollen; the surrounding skin is œdematous, and the disease may involve the big toe on the other foot, or less commonly other joints. In about a week the symptoms disappear and the patient often feels remarkably fit. Recurrences of acute gout follow the first attack, usually within a year, and in the absence of treatment and attention to diet and regime may become increasingly frequent.

Chronic Gout.—After a number of repeated attacks of acute gout a condition arises in which there is never complete relief from symptoms. The joints, especially those of the big toes, of the tarsus, and of the fingers, are much deformed; tophi appear in the cartilages of the ears or around the joints, and there is often swelling of the olecranon and prepatellar bursæ. Suppuration rarely occurs, although the chalky material may ulcerate through to the surface.

The sufferer from gout, whether in the acute or chronic stage, is notoriously irritable, but yet retains his intellectual powers unimpaired. On physical examination the heart is often found to be enlarged to the left, and the blood pressure is raised. Traces of albumin are common, and if renal function tests are carried out they often reveal a diminished excretory power in the kidneys.

Many other symptoms occurring in patients, with or without obvious gout, have been ascribed to "suppressed gout" or a "gouty diathesis." Among these are eczema, brittle nails, conjunctivitis and iritis.

Diagnosis.—Chronic gout with deformity of the joints may be misdiagnosed as rheumatoid arthritis, but the presence of tophi, the X-ray appearances, and a raised blood uric acid should help to avoid confusion. Recovery of function in gouty joints is much more rapid than it is in cases of infective arthritis.

Treatment.—Sufferers from gout or even those with a family history of the disease should be specially abstemious as regards both food and drink. By reasonable physical activity and dietetic restriction they should endeavour to keep themselves well below average weight.

Foods which contain excess of purins, such as sweetbreads, kidneys, and liver, are forbidden. Meat may be allowed in moderation but the diet should mainly consist of vegetables, bread, fresh fruit, and cheese. Most though not all gouty subjects find from practical experience that beer and wine bring on attacks.

During acute attacks the affected limb must be covered with cotton wool and the pressure of the bed-clothes avoided by the use of a cradle. Hot fomentations or lead and opium lotion may be applied locally. Colchicum is almost specific in relieving the pain. The drug is best given in the form of the alkaloid colchicine. The initial dose is $\frac{1}{60}$ gr. (1 mg.), followed at two-hourly intervals by doses of $\frac{1}{120}$ gr. ($\frac{1}{2}$ mg.). The drug is taken as a pill. It is continued until the pain is relieved or toxic symptoms develop. The latter are diarrhœa, nausea, and vomiting. As a rule the pain of acute gout disappears in twenty-four to forty-eight hours under this regime. The patient should take at

least five pints of fluid daily and the bowels should be kept open with saline purgatives. If colchicine is not available, tincture of colchicum may be given (15 minims) four hourly in an alkaline mixture.

In chronic gout the excretion of uric acid may be effected by large doses of sodium salicylate (100 gr. daily, given with alkali) or by aspirin (60 gr. daily). This should be continued for several weeks. Cinchophen (atophan) is also sometimes effective but occasionally produces toxic jaundice. It is given in 7½ gr. doses thrice daily for three days and should then be omitted for six days. It is a potentially dangerous drug and should be taken only under close medical supervision. It should not be given to patients with cardiovascular or renal disease, nor to those with any evidence of hepatic insufficiency.

OBESITY

The disadvantages, or rather the dangers, of obesity have only been fully realised within comparatively recent years. Even at the present time overweight is still only too often regarded by the layman as an indication of robust health.

Needless to say, there is no satisfactory formula for ascertaining the ideal weight in relation to age, sex, and height. The experience of life assurance companies is embodied in the table given in the Appendix on Life Assurance Examination (*vide* p. 848). Though the figures in the table give an indication of the average weights, a person even 20 per cent. above the tabular weight is not necessarily unduly obese.

The best criterion of obesity is not so much the patient's weight as his or her appearance. The general build, and in particular the abdominal girth in relation to the chest measurement, are perhaps the most reliable guides. When the abdominal measurement exceeds that of the unexpanded chest, the individual may always be regarded as too fat.

No one likes to be accused of obesity, and it is rare to meet any person, however fat, who will admit to overeating as a causative factor. The patient prefers to ascribe the condition to familial predisposition, while the physician often postulates somewhat hypothetical disorders of the endocrines. Though undoubtedly pathological obesity may occur as the result of endocrine upset, it is probably true to say that overeating and a sedentary life account for the majority of cases. Heredity is also a potent factor.

It is often stated that alcohol produces obesity. To a certain extent this is true, at any rate, as regards the chronic beer drinker. Too often, however, the total abstainer and non-smoker in compensation for his self-denial is apt to consume a diet quite out of proportion to his needs, which often includes an excessive amount of sweets and chocolate.

Exercise is more effective in the prophylaxis than in the cure of obesity, for, unfortunately, once the condition is well established a vicious circle is set up, as the physical disabilities induced by obesity forbid adequate exercise.

Dangers of Obesity.—The statistics of life assurance companies prove quite conclusively that the unduly obese are bad lives. The special dangers are classified below :—

1. Operations, especially abdominal, are notoriously more difficult and dangerous in the obese than in the spare individual. Moreover, the prognosis in acute infections, such as pneumonia, is distinctly unfavourable in the obese.

2. Diabetes is very frequently associated with obesity.

3. Cholecystitis and gall-stones are more common in obese than in spare persons.

4. Osteo-arthritis, particularly in the lower extremities.

5. Varicose veins are frequently troublesome.

6. Fatty degeneration of the heart, hypertension, and angina frequently accompany obesity, as also do chronic bronchitis and emphysema.

Obesity in Endocrine Disorders.—The thyroid and pituitary glands are known to influence fat metabolism. Hypothyroidism or myxœdema is always associated with some degree of obesity, as are certain anomalies of pituitary secretion, such as Fröhlich's and Cushing's syndromes. At the menopause there is often a tendency for the weight to increase rather rapidly, perhaps as a result of ovarian hypofunction. Similarly, castration results in adiposity, which is also common in the adreno-genital syndrome (*vide* p. 219).

Treatment.—In obesity, not obviously related to disorders of the endocrine glands, much can be done by readjustment of the general regime, especially as regards diet. The constituent of food which is mainly responsible for the production of obesity is carbohydrate, and this, therefore, needs to be restricted in anti-obesity diets. The factor limiting this restriction is the palatability of the diet, and it is usually necessary to give up to 120 gm. *per diem*. As it is desirable that the patient should consume his own fat, the intake of fats must be severely restricted. It is usually impossible to cut down this to below 40 to 50 gm. *per diem*. Proteins may be taken in normal amounts as they are not productive of obesity in themselves and also have a tendency to increase metabolism.

The following diet has been proved effective in the Dietetic Clinic at the Royal Infirmary, Edinburgh, and is not unpalatable :—

Approximately : CHO = 116 ; Pro. = 70 ; Fat = 52 ; Calories = 1,200.

Breakfast—

Tea or coffee with milk from ration.
1 orange or half grapefruit.
1 oz. brown bread (one thin slice), or 2 Ryvita or Vitaweat biscuits.
1 egg or 1 oz. (one thin slice) of lean ham or tongue.
Butter from ration.

Dinner—

Bovril, Oxo, or clear soup *ad lib.* if desired.
An average helping (2½ oz.) of any lean meat (except pork), fish (not fried), poultry or game (except goose or duck), or rabbit.
Large helping of any vegetable, except potatoes, peas, beans, or lentils.
Fresh salad when possible (no oil or cream in dressing).
Fruit, 4 oz. of 10 per cent. group (*vide* p. 241).
½ oz. (one section) cheese.
2 water biscuits, or ½ oz. (half thin slice) brown bread.
No sweet wine, beer, stout, spirits, or aerated waters.

Tea—

Tea with milk from ration.
1½ oz. brown bread (one and a half thin slices) made into a sandwich with tomato, lettuce, or cress.

Supper—

Bovril, Oxo, or clear soup *ad lib.* if desired.
Average helping (2½ oz.) lean meat, fish, etc., as at dinner.
Vegetable and fruit as at dinner.
½ oz. brown bread (half thin slice) or 1 Ryvita biscuit.

Daily—
Butter, $\frac{3}{4}$ oz.
Milk, $\frac{1}{2}$ pint.
No sugar to be used—saccharine can be substituted if desired.
Drink plenty of water in between meals.

The following articles should be completely forbidden : all forms of sugar, chocolates, jam, and the like ; potatoes ; green peas ; all starchy foods such as rice or macaroni. The fat-containing fish, such as sardines and salmon, are better avoided. The intake of salt should be limited to that used in cooking. Consumption of beer, stout, and sweet wines, such as port, must be stopped, but spirits in small quantities or light wines, such as claret, probably do no harm. Fluids can be taken in normal amounts but are best drunk between rather than with meals.

In conjunction with dietetic restrictions on the above lines an attempt must be made to encourage physical exercise, which need not, however, be violent. If the patient is both elderly and obese, undue exercise is likely to be not only ineffective but dangerous.

The value of drugs in obesity is doubtful, except where there is definite evidence of endocrine disorder. Many proprietary remedies contain thyroid and if used indiscriminately may be dangerous. No patient should be allowed to take thyroid except under close medical supervision. It must be remembered that its action is to some extent cumulative. The citrates are often prescribed but there is little evidence that they have any effect. Dinitrophenol preparations are definitely dangerous and should never be given.

In obesity following the menopause, thyroid extract is often effective not only in controlling the weight but in the alleviation of the manifold symptoms so often present at that period. The dose may need to be gradually increased up to 5 gr. a day or more. Thyroid is also extremely valuable in myxœdema. Pituitary extract is, however, probably completely ineffective in obesity due to disorders of that gland.

Unfortunately it is easier to give instructions as to diet than to see that they are carried out. Rigid adherence to a diet which will produce steady loss of weight needs, as a rule, more determination and self-control than the average subject of obesity can muster. Hence the value of spa treatment with its strict dietetic control and routine exercise. Under a satisfactory dietetic regime about 2 to 3 lbs. should be lost weekly. Too rapid a loss may produce lassitude and exhaustion.

Adiposis Dolorosa (*Dercum's disease*).—This condition occurs chiefly in middle-aged females, who become enormously obese, and develop diffuse and often symmetrical masses of fat on the trunk and limbs, which are extremely tender on pressure. In addition the patient is usually depressed and emotional, and the obesity leads to asthenia. Although adiposis dolorosa has been attributed to pituitary dysfunction there is no evidence in support of this view. Treatment is unsatisfactory but dieting and thyroid extract may be tried.

VITAMIN DEFICIENCY DISEASES

The vitamins are accessory food factors necessary for normal growth and the maintenance of health. They may be conveniently divided into two main

groups, water-soluble and fat-soluble. Vitamins of the same group are found in similar foodstuffs, so that single vitamin deficiencies rarely, if ever, occur in clinical practice. The relative degrees of deficiency of each of the vitamins differs in nearly every patient, since few people take exactly similar diets ; as a result of this, the clinical features of the vitamin deficiency diseases show great variations.

There is a considerable amount of evidence that many of the vitamins are synthesised in the gut by the bacterial flora in sufficient quantity to affect very materially the daily intake. This is one of the reasons for the marked variations found between individuals in their response to exactly similar deficient diets.

Several vitamins can now be synthesised and the existence of others has been proved, but our knowledge is far from complete and there is little doubt that many more vitamins remain to be discovered.

Consideration of the foregoing facts makes it clear that the essential measure in therapeutic or prophylactic treatment must be to provide an adequate diet of natural foodstuffs, and that synthetic vitamins should only be used to help in relieving acute gross deficiencies and to act as incomplete substitutes when the necessary natural foods are not available or cannot be assimilated.

Much has been written on " sub-clinical " deficiencies during the past few years, but the available evidence tends to show that there is a wide margin of safety, and health is not impaired until gross deficiency is present. The first appreciable effect of experimental deficiency of most vitamins is the onset of various subjective symptoms, such as lassitude, depression, irritability, weakness, anorexia, insomnia, and possibly an increased susceptibility to infections ; clinically these symptoms are far more commonly due to other causes and are therefore of little help in the diagnosis of early vitamin deficiencies.

Two important deficiency diseases—rickets and infantile scurvy—are described in the section dealing with diseases of infants (*vide* pp. 184, 183).

The fat-soluble vitamins are :—

Vitamin A.—Present in butter, eggs, and all animal fats, and synthesised in the body from carotene, a red pigment found in certain vegetables, especially carrots.

The early manifestations of vitamin A deficiency are the keratinisation of epithelial tissues and the development of night-blindness. The former effect usually first appears as follicular hyperkeratosis of the skin. Night-blindness can be due to a pure vitamin A deficiency, but recent work suggests that deficiency of other vitamins may play a considerable part in its production. It must be remembered that factors unconnected with any vitamin deficiency can also be responsible for night-blindness. In children, lack of vitamin A results in imperfect formation of the enamel of the teeth. The average approximate daily requirement of vitamin A is 4,000 international units, or 14,000 i.u. as carotene.

Vitamin D.—Present in animal fats. Deficiency in children gives rise to rickets (*vide* p. 184). There is little known about the role of vitamin D in adults.

Vitamin E.—Present in vegetable oils, especially wheat-germ oil. There is considerable evidence that vitamin E is beneficial in some cases of recurrent abortion.

Vitamin K.—Present in kale, spinach, and other vegetables, it requires the presence of bile-salts for its absorption from the gut, and is therefore liable to become deficient in cases of obstructive jaundice. It is essential for the formation of prothrombin in the liver, and given parenterally to patients with obstructive jaundice it prevents their abnormal tendency to bleed, provided there is no gross liver damage. It is of value in hæmorrhagic disease of the newborn, where the prothrombin level is low.

The water-soluble vitamins :—

Vitamin B Complex.—Includes several known factors and probably others not yet identified. Here only vitamin B_1 and two members of the vitamin B_2 complex, riboflavin and nicotinic acid, will be considered.

The chief sources of the members of the vitamin B complex are whole-wheat (not white flour), yeast, vegetables, and dairy products.

Vitamin B_1 (Aneurin).—The early signs of deficiency of this vitamin are palpitations, tachycardia, loss of vibration sense in the legs, tenderness of the calf muscles, and the loss of reflexes. The average daily requirement is 1 to 2 mg.

Vitamin B_2.—*Riboflavin.*—Several conditions result from deficiency of this vitamin. The lips develop a deep vermilion colour with a thin, shiny, and denuded mucosa, a condition known as cheilosis. Painful ulcerations occur at the angles of the mouth (angular stomatitis) and these may have a superimposed monilia infection when the condition is called perlèche. The tongue is clean, but sore, and is usually purplish red with enlarged flattened papillæ. The approximate daily requirement is 1 to 3 mg.

Eye lesions are sometimes the earliest signs and consist mainly of corneal vascularisation with photophobia and itching and burning of the eyes.

Nicotinic Acid.—The earliest lesions in cases of deficiency of this vitamin are a glossitis in which the tongue is sore, clean, fiery red, and shiny, and a dermatitis on exposed parts of the body. The later lesions are described under pellagra. The approximate daily requirement is 20 to 40 mg.

The evidence in support of claims for the existence of a causative relationship between nicotinic acid deficiency and infections with Vincent's organisms is far from conclusive.

Vitamin C (*vide* p. 225).—Approximate daily requirement is 25 to 50 mg.

Beri-beri and Pellagra

In the past there have been many theories about the ætiology of these two diseases, but it is now recognised that both are essentially due to vitamin deficiencies, although certain other factors may be contributory causes. In recent years beri-beri has been said to be due to vitamin B_1 deficiency and pellagra due to nicotinic acid deficiency. It is now considered that both these diseases are due to a multiple B-complex deficiency, beri-beri being produced when the deficiency of vitamin B_1 is dominant, and pellagra when nicotinic acid is mainly deficient. This theory is supported by the fact that a deficiency of only one member of the B-complex is extremely unlikely and that beri-beri and pellagra show great variety in their symptomatology, many of the symptoms being common to both diseases ; probably riboflavin deficiency plays an important role in both. In fact, it is best not to look upon beri-beri and pellagra as two definite diseases, but rather as convenient labels for the two extremes of all the symptom-complexes found in vitamin B complex deficiency.

Beri-beri

Morbid Anatomy.—The post-mortem findings are those associated with cardiac incompetence and peripheral neuritis, the nerves of the legs being particularly affected.

Symptoms.—Either the cardiac or neuritic lesions may predominate, giving rise to " wet " or " dry " beri-beri respectively.

The onset of beri-beri is insidious ; early symptoms are weakness or a feeling of weight in the legs, palpitation, and dyspnœa. The knee jerks are diminished and ultimately completely lost ; symptoms referable to sensory nerves also occur in the form of paræsthesiæ, patches of cutaneous anæsthesia, and tenderness of the calves. The weakness of the legs gradually increases, and there is obvious muscular wasting, unless this is obscured by œdema. The muscles show the reaction of degeneration.

The heart is always enlarged, and there is often a marked engorgement of the veins. Occasionally cardiac failure occurs early and results in sudden death.

Diagnosis.—The combination of peripheral neuritis with œdema presents a picture seen in no other disease. It is important, however, to avoid overlooking cases where the main symptoms are neuritic. Tenderness of the calves, diminution of the knee jerks, and areas of paræsthesia or anæsthesia should arouse suspicion of beri-beri when they occur among persons whose diet is open to suspicion.

Treatment.—As in all disease, prevention is better than cure. and the provision of food containing the vitamin B complex is a sure protection against beri-beri. The most satisfactory method of supplying the deficiency, in armies or on board ship where fresh food is difficult to obtain, is to substitute whole-meal for white bread. If rice forms the staple article of diet, as it does in many eastern countries, it should be undermilled in order that part of the vitamin-containing husk may be retained.

When there is evidence of cardiac involvement, the patient must be strictly confined to bed, and careful nursing is essential. A mixed diet with milk, fresh meat, and vegetables must be ordered, and in addition, yeast and whole-wheat should be added to the diet to supplement its vitamin content. Several proprietary preparations of vitamin B_1 (aneurin) are available and can be given either by mouth or by injection, but it must be remembered that this is not the only vitamin which is deficient. In acute attacks as much as 50 mg. of aneurin intravenously and repeated at eight-hourly intervals may be required.

Pellagra

Pellagra is a chronic disease characterised by gastro-intestinal and nervous symptoms, and an erythematous rash.

Symptoms.—The most characteristic, though not necessarily the earliest, manifestation of the disease is an erythematous rash of somewhat peculiar type and distribution. In its early stage it resembles an erythema, such as may be produced by sunburn or a mustard plaster ; later, the skin becomes thickened and resembles parchment, and there is often pigmentation with desquamation of the epithelium. The rash is most commonly seen on the parts of the body exposed to sunlight, particularly the back of the hands and around the wrists and neck ; the extensor rather than the flexor surfaces are

affected. The skin condition starts most commonly during the spring and tends to disappear after a few months, only to recur during the following spring.

The gastro-intestinal tract is often affected. Vague digestive disturbances, such as flatulence and eructations, are common; the tongue is red and desquamated, and the patient frequently complains of a burning sensation in the mouth; there is persistent diarrhœa in the later stages.

The most serious feature of the disease is the involvement of the central nervous system, which tends to occur in the more chronic and severe cases, many of whom ultimately end their days in an asylum. Subjective symptoms such as depression, insomnia, and headache are common, and not infrequently these progress to a definite dementia with hallucinations and delusions, which may necessitate certification. Lesions of the spinal cord may occur similar to those of subacute combined degeneration; these may give rise to spastic or flaccid paralysis, and increase or loss of the tendon reflexes.

Diagnosis.—This rests mainly on recognition of the rash, which in most cases is typical. Sprue is distinguished by the characteristic bulky and fatty stools.

Treatment.—A good mixed diet with the addition of yeast and with plenty of fresh fruit and green vegetables will frequently effect a cure by itself.

Administration of nicotinic acid in 50 mg. or larger doses after meals, a daily dosage up to 500 mg. being given, is usually rapidly effective. But the cure will not be permanent, even if the nicotinic acid is continued, unless the general deficiency of the vitamin B complex is given adequate attention.

SCURVY

Vitamin C (Ascorbic Acid).—This substance is water-soluble, and is rapidly destroyed by heat when in alkaline solution. It is present in all fresh fruits and vegetables, especially lemons, oranges, and tomatoes. Although potatoes are not very rich in vitamin C, they supply a very large part of the daily requirement wherever they form a staple food owing to the large quantity consumed. In recent years good results have been claimed for the treatment of many diverse conditions with ascorbic acid, but little conclusive evidence has been produced to support most of these claims. Gross deficiency of vitamin C results in scurvy and deficient wound healing, but all the evidence tends to show that a patient has to be almost scorbutic before any lack of wound healing is revealed.

Scurvy has been one of the great scourges of armies in the field, and it was the dread of seamen on long voyages until the preventive qualities of lemons were discovered. At the present time the disease is rare in adults, but it is still relatively common in infants in whom it produces a rather different clinical picture, which is described as infantile scurvy, or Barlow's disease (*vide* p. 183).

Pathology.—The most striking feature of the disease is a tendency to hæmorrhage, so that extravasation of blood and petechial hæmorrhages may be found in any part of the body. This hæmorrhagic tendency is associated with a loss of and an inability to re-form intercellular matrix.

Symptoms.—The onset of scurvy is usually insidious, with pallor, lassitude, and dyspnœa as early symptoms. If the dietetic deficiency is not corrected, more characteristic symptoms develop. The most striking of these is the

condition of the gums, which become congested and spongy and bleed readily. As the disease progresses the swollen gums may almost completely envelop the teeth, which become loose, and may ultimately fall out. It should be noted that the gums of edentulous scorbutic patients usually remain normal. At the same time petechial spots appear on the skin, particularly on the legs, together with larger ecchymoses. Sometimes hæmorrhage takes place in the substance of a muscle producing a hard brawny swelling, tender to the touch. Other manifestations of the hæmorrhagic tendency are subperiosteal hæmorrhage. Uncomplicated scurvy is apyrexial, but sufferers from it are very liable to intercurrent infections and frequently die of pneumonia. In the later stages there are œdema of the legs and sometimes effusions in the pleura and pericardium.

Diagnosis.—In the presence of many cases, diagnosis is easy, but with sporadic cases there may be confusion with purpura hæmorrhagica. In cases of doubt a blood platelet count may be helpful, as in scurvy the count is high, while in purpura it is often very low. The therapeutic test is also a valuable aid in diagnosis, for a patient with scurvy, when put on a diet rich in vitamin C, shows a rapid improvement.

Prophylaxis and Treatment.—Where there is no poverty and a mixed diet is eaten there is little risk of scurvy among adults. Where it is impossible to get suitable food, a ration of lemon juice is an effective prophylactic. Scurvy sometimes occurs in patients on a restricted diet, such as those on strict dietetic treatment for peptic ulcer.

The symptoms disappear with marvellous rapidity when the patient is put on a diet with an ample surplus of fresh fruit, particularly oranges and lemons, fresh milk, cabbage, salads, tomatoes, and potatoes. The vitamin is destroyed by alkalis and the use of soda in cooking green vegetables increases the rate of destruction. Scurvy can be rapidly got under control by giving ascorbic acid either by mouth (150 to 300 mg. daily) or by injections in amounts up to 500 mg. in urgent cases. Some cases have, however, been reported which did not respond to the synthetic ascorbic acid, but recovered rapidly on orange juice. It is important always to attend to the diet, as probably all cases are deficient in other vitamins as well.

Patients with scurvy should be kept in bed until marked improvement has taken place, in view of the risk of sudden syncope and heart failure, even on slight exertion. For pain or restlessness, morphia may be necessary.

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DISEASES OF THE BLOOD, LYMPHATIC GLANDS, RETICULO-ENDOTHELIAL SYSTEM, AND SPLEEN

DISEASES OF THE BLOOD

Physiology

TO understand many of the features presented by the diseases discussed in this section, it is essential to remember certain physiological points concerning the circulating blood, and the mechanism by which departures from the normal may occur.

When interpreting blood counts, not only must we appreciate what may be called " normal variations," but also remember the most acceptable theories concerning the origin of the various cells in the blood. The red cells consist of a stroma or framework, composed chiefly of protein material, containing in its meshes hæmoglobin. They are of about 7·2 μ average diameter, form about 50 per cent. of the total mass of the blood, and total in men about 5,000,000 per cubic millimetre or slightly more, and in women about 4,500,000. The total surface area of the corpuscles is about 3,000 square metres, or 1,500 times the surface of the body itself—a point of some importance in facilitating oxygen interchange. In the adult the red cells are derived from the red bone marrow, which contains all their precursors. Red cells, as seen in a blood film, may show abnormalities of the following types : (i) Shortage of iron intake or excessive loss (hæmorrhage) may cause the cells to be poorly filled with hæmoglobin, pale and somewhat irregular in shape. (ii) A sudden call for large numbers of new cells, as after a large hæmorrhage, may result in the premature turning into the circulation of polychromatic or young cells (*reticulocytes*), or immature cells with small round nuclei (*normoblasts*). (iii) Some pathological process directly affecting the bone marrow (as in pernicious anæmia, leukæmia, etc.) may prevent the proper maturation of the reds, which therefore appear in the circulation in their quite immature forms (*megaloblasts*, *erythroblasts*, etc.). (iv) Some toxic substance may be actually taken up by the red cell and produce a characteristic microscopical appearance, *e.g.*, the punctate basophilia of lead-poisoning.

Two types of white cell are easily distinguished, namely, the granulocytes having granular cytoplasm (neutrophil polymorphs, eosinophils, and basophils) and those without granules (lymphocytes). In the main, granulocytes are formed only in the bone marrow, and lymphocytes only in lymphatic tissue. Both these tissues form part of the reticulo-endothelial system of cells. Any disturbance of this system, as in leukæmia, is especially liable to distort the patient's white count. On the other hand, the more common changes in the white count are physiological responses to abnormal stimuli. For example, the granulocytes which are mainly phagocytes show increased production in septic states, such as pneumonia, where cellular debris has to be removed from the tissues. Again, the increase in lymphocytes

in tuberculous infection is simply an indication of the glandular hyperactivity which is part of the natural defensive reaction. Immature white cells may appear in the blood if there is a very sudden and vigorous call for any particular type. In the case of the granulocytes (polymorphs), a satisfactory defensive response results in the appearance of many "young" forms. As the younger the cell the fewer the lobes seen in its nucleus, this can be recorded as the *Arneth count*, which is a percentage record of the number of cells having one to five lobes to their nuclei. Normally, the greatest number have two, three, or four lobes. In a vigorous defensive leucocytosis the majority may have only two, while many young forms with only a horse-shoe shaped, unlobed nucleus will occur. This change in predominance is described, according to the customary method of recording (Arneth count), as the "shift to the left." In the case of deficient white-cell production, such as occurs in pernicious and aplastic anæmias, the predominant cell may be older and therefore possess more nuclear lobes, in which case the count shows a "shift to the right."

The frankly immature cells, namely, myeloblasts and myelocytes, appear with any frequency in the circulating blood only when there is gross disturbance, general or local, of some part of the blood-forming system. Their appearance represents failure in function and in proper maturation, and never occurs as a physiological response to external stimuli.

A valuable direct method of determining the nature of any developmental failure in either red or white cell production is biopsy of the bone marrow by *sternal puncture*. Thin films of fresh bone marrow are immediately fixed and stained. The percentage occurrence of all types is recorded as a *myelogram*, at least 500 cells being counted. From these records, comparing it with the average normal figures, direct evidence is obtained as to which phase of erythropoiesis is at fault. The characteristic findings in different blood diseases are later mentioned in their appropriate sections.

The platelets remain to be considered. They arise from the bone marrow during the development and differentiation of the megakaryocytes and are intimately concerned with coagulation. They influence, however, not the production of the fibrin clot as such but its proper contraction and firmness. Without a full quota of platelets, clots are not efficient in closing breaches, traumatic or toxic, in the capillary walls. The normal count is about 250,000 platelets per cubic millimetre. Increases above this level, such as may occur in puerperal states, produce liability to thrombosis, whereas falls to about 40,000 per cubic millimetre result in purpura and extensive bruising from quite trivial trauma. At about 15,000 per cubic centimetre there is a tendency to spontaneous hæmorrhage from mucous membranes.

In this connection determination of the *bleeding time* and *clotting time* may be of the greatest importance. The bleeding time is that taken for oozing to cease from a sharp single finger-prick made with a Hagedorn cutting needle. According to the depth of the prick, bleeding will cease in a normal person in three to four minutes. Variations depend upon the rate of clot retraction as well as upon actual coagulation. Thus when there is a platelet shortage, formation and fixation of an efficient clot is delayed, and therefore the bleeding time is prolonged, although the rate at which the first actual coagulum forms may be normal. To determine the clotting time, the most satisfactory method is that of Laidlaw. By this method the normal clotting time is three to four minutes. For accurate observations in patients with

liver damage and those receiving such coagulation-retarding drugs as dicoumarin, the *prothrombin time* is estimated. Calcium and excess of thromboplastin as Russell viper venom (stypven) are added to the plasma, the speed of the resultant clotting then being proportional to the prothrombin content. The normal time is about 15 sec.

Red Cell Sedimentation Rate.—When a column of freshly collected, citrated blood is set up, the *rate* at which the red cells sink down to form a compact layer depends upon variations in the plasma proteins, which are in turn related to the presence or absence of tissue breakdown proceeding in the body. The more active the tissue change, the greater the rate of fall of the red cells, and the test becomes a delicate indirect method of detecting the activity or quiescence of inflammatory processes not readily observable by direct means. The normal blood sedimentation rate is 1 to 8 mm. in one hour (Westergren's method).

The subject of blood groups is discussed later in connection with blood transfusion.

The *specific gravity* of blood is normally about 1,059. In anæmia this figure may be much lower. In collapse, or conditions in which great loss of fluid occurs, *e.g.*, cholera, a marked rise may be noted.

Normal red cells can resist the osmotic pressure set up when they are immersed in saline of 0·45 per cent., isotonic saline being 0·9 per cent., and are not laked until they are immersed in weaker saline solutions. The highest dilution which any particular cells can resist is taken as a measure of their *fragility*, a determination of great diagnostic value in acholuric jaundice, in which condition the cells are unusually fragile.

The average quantity of hæmoglobin in the blood of healthy adult males is about 16·2 gm. per 100 c.c. The average red cell count in the normal male is actually nearer to 5,500,000 than 5,000,000 cells If we take, as is usual, only 5,000,000 per cubic millimetre as the "normal," then for purposes of estimating the *colour index* (*vide* p. 269), which is $\frac{\text{Hæmoglobin percentage}}{\text{Red cell percentage}}$, the "normal" or 100 per cent. hæmoglobin figure as marked on the hæmoglobinometer scale should correspond to about 14·5 gm. of hæmoglobin per 100 c.c. Unfortunately the absolute value of 100 per cent. varies with the type of instrument. In the Haldane it is only 13·8 gm., in the Sahli and Hellige acid hæmatin types it is about 14·7 gm. Therefore, for routine clinical purposes, the acid hæmatin standard is now generally used. Then if the "normal" red count is taken to be 5,000,000 per cubic millimetre, the figure for the colour index will be truly representative, as it is meant to be, of the relative amount of hæmoglobin per cell, 1·0 being the normal index. The hæmoglobin contained in an average red cell, the *mean corpuscular hæmoglobin*, can be expressed as the weight of hæmoglobin in 1,000 c.c. of blood (147 gm.) divided by number of cells in millions per cubic millimetre (5·0) giving a normal value of 28·2 micro-micrograms of hæmoglobin per cell.

The *average diameter of the red cells* in films, normally about 7·2 μ, is, together with the colour index, raised in megalocytic and reduced in microcytic anæmia. It may be determined either directly by Price-Jones projection methods or indirectly by halometer, a small halo resulting from the large cells and vice versa.

By use of the Wintrobe hæmatocrit or similar apparatus it is possible to

determine the mean volume of the packed red cells. The tube filled with fresh heparinised blood up to the 100 mark is centrifuged at 3,000 revolutions per minute for 15 minutes or until the red cell level ceases to fall. Normally the top of the column reads about 46, *i.e.*, the volume of packed red cells per 100 c.c. of blood is 46 c.c. The *mean corpuscular volume* is then given when the volume of red cells in 1,000 c.c. of blood (460 c.c.) is divided by red count in millions (5·5), *i.e.*, normally about 84 cubic microns.

The occasions when these estimations are clinically helpful are referred to in later sections.

Blood Transfusion

Although the idea originated centuries ago, it is only during the last thirty years that transfusion of blood has become relatively safe and simple. This results from two discoveries : a knowledge of the blood groups and the use of sodium citrate as an anticoagulant. Without a knowledge of blood groups, transfusion was at best a hazardous operation. Without citrate methods the technique of the operation was necessarily difficult owing to the risk of clotting.

Blood Groups.—The existence of " blood groups " in human beings was first shown by Landsteiner in 1901. In 1907 Jansky described four distinct groups. Two years later Moss published his classification of bloods into arbitrarily named Groups I to IV. The Moss grouping was widely used for many years, but has now been universally superseded by the International (A, B, O) Classification. The red cells of any particular person carry both, one, or neither of two agglutinogens A and B, making four possibilities, AB, A, B, and O. Contact between cells carrying A or B and any serum containing the corresponding agglutinins, termed respectively α and β, will result in agglutination of the cells. Four stable mixtures may therefore be met with, namely, $AB + o$, $A + \beta$, $B + \alpha$, and $O + \alpha\beta$. These are the four main blood groups which for simplicity are named by their cell agglutinogens only. For bloods from different individuals to be completely compatible they must belong to the same group. But in transfusion practice, although it is essential that the ingoing cells of the donor shall not be clumped by the recipient's serum, any agglutinins in the donor's serum are too diluted to affect appreciably the patient's own cells. Therefore it is possible to use as donors not only persons of the same group as the patient but also any, namely, the " universal " group O donors, whose cells will be unaffected by agglutinins in the patient's serum. The table given on page 261 will make this more clear.

Before transfusion, therefore, it is essential to know the group of both donor and recipient. The technique of grouping, using the " four group " classification, is simple. Fresh high-titre specimens of known Group A and Group B sera are required, and can nowadays be obtained from the official serum laboratories. A little of the blood to be tested is collected from a finger-prick into a tube containing a small quantity of 3 per cent. sodium citrate. A drop of the cell suspension thus obtained is mixed on a perfectly clean glass slide with separate drops of the two known sera. The drops are kept under observation for ten to fifteen minutes, preferably at 37° C. incubator temperature, but this warming is not usually necessary. When agglutination of the cells occurs they clump together, the even emulsion taking on the appearance of coarse grains of red pepper lying in the clear

serum. The change is readily seen with the naked eye when the slide is examined against a white background. By reference to the table it will be seen that should no agglutination occur with either serum, the cells tested are of Group O. If there is agglutination with both sera, the cells are of Group AB. If the cells agglutinate in serum A only, they are of Group B. If they

Donor's Blood.	Moss Groups.	International Classification.		Percentage Occurrence.	Recipient's Blood.			
					Agglutinins in Serum.			
					o	β	α	αβ
		Agglutinogens in Cells.	Agglutinins in Serum.		Agglutinogens in Cells.			
					AB	A	B	O
	I.	AB	*o*	7	−	+	+	+
	II.	A	β	40	−	−	+	+
	III.	B	α	10	−	+	−	+
	IV.	O	αβ	43	−	−	−	−

Table showing the result of the cells of donors of the various groups being brought into contact with the sera of the four possible types of recipient. A plus sign implies agglutination of the donor's cells, a minus sign the absence of agglutination. The relationship between the International and Moss Classifications is shown, the percentage occurrence of the groups, and also the agglutinogen-agglutinin make-up of each variety of blood.

agglutinate in serum B only, they are of Group A. In recent years it has been found possible to divide this last group into A_1 and A_2. But this subdivision need not affect transfusion technique except in so far as occasional cases of Group A_2B have a serum which agglutinates O cells and thus introduces a slight risk of untoward reaction if a universal O donor is used for an AB patient without preliminary cross-matching. In all cases of doubt, the M.R.C. Memorandum now advises a test-tube technique. In " grouping " a patient or donor both cells and serum are tested. Clotted and citrated blood samples are needed, also standard Anti-A and Anti-B sera as well as 5 per cent. suspensions of known A_1, A_2, and B cells. In small tubes equal parts of the known and unknown sera are separately mixed with equal parts of the known and unknown cell suspensions. All combinations are thus tested and grouping becomes certain. The tubes stand at room temperature for two hours and agglutination is read through a hand lens. Cross-matching follows similar lines, clotted and citrated blood being needed from both patient and donor. For satisfactory grouping tests it is essential that the samples of standard sera should be quite fresh or have been kept in the ice chest, because rapid deterioration takes place at room temperature.

The ideal donor is an individual of the same group. In these circumstances the two bloods will " cross-match " perfectly. When the donor, according to preliminary grouping, is suitable but not of the same group as the patient, one should make quite sure that the ingoing cells will not be agglutinated by the recipient's serum. In some severe disorders of the blood and very ill patients it is advisable always to use a donor of the same group cross-matching perfectly. Occasionally cases are met with whose

red cells undergo auto-agglutination even in normal saline. It is then necessary to perform the cross-matching tests at 37° C. In emergency, when precise grouping is impossible, the finding that the donor's cells are unaffected by the patient's serum will justify transfusion.

One or both of two additional agglutinogens, termed M and N, may be present in human red cells. The corresponding agglutinins are not, however, found in any natural human sera. Therefore no account need be taken of the M and N factors for blood-transfusion purposes. But specific M and N agglutinating sera can be made by animal inoculation, and therefore by use of these, as well as the known A and B human sera, twelve instead of four blood groups can be identified and termed AM, AN, AMN, BM, BN, BMN, OM, ON, OMN, ABM, ABN, and ABMN. This wider differentiation of blood samples has its obvious application in medico-legal work.

The corpuscles of about 85 per cent. of human beings contain another factor known as Rhesus (Rh.), but normally human plasma contains no anti-Rh. agglutinins. Consequently hæmolysis will not occur when Rh. positive blood is transferred into a Rh. negative recipient. There is, however, evidence that when such a transfusion has been carried out there may be a slow formation of anti-Rh. agglutinin in the recipient. If after a long interval a further transfusion from a Rh. positive donor is given, this anti-Rh. agglutinin may produce serious hæmolysis. It is probable that this is the explanation of some of the severe, sometimes fatal, reactions which occur when a patient has more than one transfusion, especially if an interval of years has elapsed between transfusions. Rh. negative patients who have had previous transfusions more than a year before should be transfused only with Rh. negative blood. In all such repeat transfusions it is wise to have the bloods of donors and recipients cross-matched by experts. The patient's serum may also be tested for Rh. agglutinins. The occasional appearance of anti-Rh. in the serum of a Rh. negative mother when she carries a Rh. positive fœtus accounts for many of the cases of erythroblastosis fœtalis (*vide* p. 177). When a liability to this condition is suspected the Rh. group of the mother and father should be determined, and also the presence of anti-Rh. agglutinins in the mother.

After any transfusion, even with a compatible blood, there is sometimes a general reaction with pyrexia and rigors, especially in debilitated or pyrexial patients. If an incompatible group is employed there is a grave risk of serious symptoms. The recipient becomes rapidly distressed and dyspnœic, suffers from precordial pain, and the pulse becomes first slow and then rapid and thready ; the temperature rises and rigors may occur ; the urine is diminished in amount, and sometimes there is hæmoglobinuria, or suppression. Death may take place rapidly, often as the result of uræmia and deposition of altered hæmoglobin in the renal tubules. If, before transfusion, the patient is given sufficient alkali by the mouth to render the urine alkaline, this deposition of pigment in the renal parenchyma is, in event of incompatibility, largely prevented. The incidence of pyrexia and rigors is reduced by (i) making sure that the blood is kept warm, its temperature never falling below 35° C. ; (ii) the use of closed apparatus for transfusion and accessory solutions which are absolutely free from living or dead bacteria and all inorganic particles ; and (iii) giving the patient ephedrine ½ gr. twenty minutes before transfusion.

The donor must not be suffering from any communicable illness such

as syphilis, malaria, or fevers in the incubation period. Allergic donors are also undesirable.

Stored Blood.—Citrated whole blood collected from the donor with absolute asepsis into closed containers and stored at 2° to 4° C. can be used without risk of undue reaction until about fourteen days after collection. Shaking must be avoided. Maizels has shown that red cells stored up to ten days become reconditioned in the patient's circulation within twenty-four hours of transfusion. But the longer the storage the more cells become changed beyond recovery and the more liable is transfusion to be followed by reactions. The leucocytes of stored blood rapidly die, and the platelets are lost by adhering to the sides of the container. Fresh blood should therefore be used for transfusing cases showing a poor white cell count and those suffering from active sepsis, acute hæmolytic anæmias, or purpura. For other types of anæmia stored blood has satisfactory replacement value.

The disadvantages of Group O blood for universal transfusion are few, but occasionally O plasma may be of exceptionally high titre and, by agglutinating the cells of patients of groups other than O, cause reactions. This also applies to the use of Group O plasma or serum.

During storage the cells settle after two days into a compact layer surmounted by relatively clear plasma. As red cell deterioration and hæmolysis begin, a pink zone appears in the lower part of the plasma and rises steadily, but this zone should not be very noticeable until about the eighth day onwards. Gross hæmolysis suggests infection of the blood. If the blood is ever allowed to freeze, it may cause severe reactions. Although stored blood should be very slowly warmed before transfusion, overheating above 40° C. causes very rapid hæmolysis and extremely severe, sometimes fatal, reactions.

Plasma Transfusion.—Systematic storage of citrated blood provides opportunity to collect and store for even longer periods large quantities of plasma. Usually samples from several donors are pooled. Drip transfusion of plasma is found to be particularly valuable when the patient is suffering from shock without hæmorrhage. The effect is to counteract the fall in plasma proteins, to restore the blood volume, and to help to raise the systolic blood pressure to the region of 100 mm. of Hg. If plasma transfusion is going to be permanently effective in this respect, marked clinical improvement will have taken place by the time 2 or 3 pints have been run in. If the patient's condition is even then not maintained, it is unlikely to be permanently benefited by further transfusion. The giving of very large volumes of Group O plasma is not without risk because, as noted in the previous section, its agglutinin content may be high.

Serum Transfusion.—Stored serum could be used for all the purposes indicated above in connection with plasma, but various practical considerations make the latter easier to handle and distribute.

Desiccation of Serum and Plasma.—Although serum and plasma can be stored wet for very long periods, drying *in vacuo* at low temperatures is the only means of ensuring really permanent preparations. Another great advantage possessed by the dried products is the enormous reduction in volume and the ease with which they can therefore be transported great distances. Before use, only simple redissolving in sterile water is required. Under active service conditions the dried products have therefore obvious advantages, but for civil hospitals they are less necessary.

Transfusion of Red Cells Alone.—If blood collected as for storage (citrate and glucose) is left for forty-eight hours in the cold the red cells will have settled into a compact layer. These can then be transfused alone, after first pipetting off the supernatant plasma. Administration should follow separation within twenty-four hours in case the blood has been infected during removal of the plasma. For the same reason the cells should be kept cold until just before use. The advantages which may lie in the transfusion of these " packed cells " are that much oxygen-carrying capacity is provided in small bulk, cardiac strain may be less and any agglutinating action of the Group O plasma upon the patient's cells is largely removed.

ANÆMIA

A diagnosis of " anæmia " is one that is often too readily made by the patient and sometimes by the medical attendant. It must be remembered that too much reliance must not be placed upon the patient's colour, for it is not unusual to find persons with a preternaturally pale complexion whose blood, as proved by estimation of the hæmoglobin, shows no evidence of anæmia. The best clinical indications of anæmia are pallor of the conjunctivæ, the nail beds, and of the palms of the hands. Needless to say, before instituting treatment for anæmia, a careful blood examination is essential.

Classification of Anæmia.—Anæmia may be due to loss or increased destruction of blood, or it may result from interference with the production of red cells. The following classification of the more common types of anæmia may be adopted :—

1. Anæmia due to loss of blood or increased blood destruction.
   - (*a*) Hæmorrhage, acute or chronic.
   - (*b*) Abnormal hæmolysis ; this includes acholuric jaundice. sickle-celled anæmia, and the acute hæmolytic anæmia of Lederer. Hæmolysis also occurs in malaria, blackwater fever, and sometimes in septicæmias.
2. Anæmia due to interference with normal blood formation.
   - (*a*) Toxic or infective processes, *e.g.*, lead-poisoning, nephritis, growths, acute or chronic infections.
   - (*b*) Deficiency anæmias : pernicious anæmia, idiopathic hypochromic anæmia, and perhaps chlorosis.

Obviously in any individual patient more than one factor may be producing anæmia ; thus carcinoma ventriculi may render the patient anæmic by continued loss of small amounts of blood, and also by its depressant effects on the bone marrow and the reduced production of the gastric hæmopoietic factor. The term " secondary " is often applied to any form of anæmia in which the colour index is low, but it is desirable to abandon this in favour of the term " microcytic " or " hypochromic," indicating that the red cells are smaller than normal and contain less hæmoglobin in contrast with the " macrocytic " or " hyperchromic " types in which the cells are on the average larger than normal and contain more hæmoglobin. In anæmias resulting from simple aplasia of blood-forming tissues, the term " normocytic " may be applied.

Anæmia due to Hæmorrhage

Very severe anæmia may result from either a single severe hæmorrhage, or from long-continued loss of smaller amounts of blood. As a rule the diagnosis is obvious, but it is important to bear in mind that bleeding from piles or from the uterus may produce a severe anæmia, though the amount of blood lost at any one time may not be very great. Treatment must be directed to the cure of the underlying condition, though in severe cases blood transfusion may be required to tide over a critical condition. Administration of iron (*vide* p. 272) accelerates the regeneration of the blood.

ACHOLURIC JAUNDICE

(*Congenital Hæmolytic Icterus*)

Acholuric Jaundice is a not uncommon familial disease which affects both sexes and may be transmitted by either. It is probable that the underlying cause of the condition is a congenital abnormality in the red cells which renders them unduly fragile. The red cells in this disease instead of being bi-concave are spheroidal (spherocytosis) and *in vitro* they show increased fragility (*vide* p. 259).

Normal red cells begin to hæmolyse in a saline solution of 0·45 per cent., and hæmolysis is complete in a 0·3 per cent. solution. In acholuric jaundice the corresponding figures are 0·6 and 0·4 per cent. This increased fragility leads to premature destruction of the cells, probably in the spleen ; the liberated hæmoglobin is transformed into bilirubin and jaundice results. The urine contains an excess of urobilin *but no bile pigment.*

Clinical Picture.—There are recurring attacks of jaundice, which usually start in childhood. The spleen is considerably enlarged and hard. Often there are long remissions followed by periods of increased hæmolysis with pyrexia, jaundice, anæmia, and sometimes a tendency to petechial hæmorrhages and ecchymoses.

Examination of the blood shows spherocytosis with a low average red cell diameter ; the degree of anæmia is variable and owing to the shape of the cells the colour index is sometimes high. Reticulocytes are numerous, often 20 per cent.—an indication of active generation of new cells to replace those lost by hæmolysis, and the van den Bergh reaction shows an indirect positive.

Pigment stones may form in the gall-bladder and are present in about 50 per cent. of cases. Often they cause no symptoms, but if they pass into the bile-duct there may be attacks of biliary colic and obstructive jaundice. During exacerbations there may be a polymorphonuclear leucocytosis, sometimes with a few myelocytes.

In long-standing cases large chronic ulcers may form on the legs, which fail to react to any form of treatment except splenectomy.

Differential Diagnosis.—Some cases of acholuric jaundice show no obvious increased fragility of the red cells and may be confused with pernicious anæmia. The family history, large hard spleen, and the numerous reticulocytes will usually make the diagnosis clear. Even when other members of the family have no obvious symptoms, examination may show that they have enlarged spleens or increased fragility.

Treatment.—Some cases have negligible symptoms and may be discovered only at a routine examination. In such no treatment is required. Those who have more severe symptoms should be advised to have splenectomy performed. Although after the operation the increased fragility may persist, the symptoms disappear and the patient remains in perfect health. If biliary calculi are present they should be removed, but the gall-bladder should be left, unless obviously infected.

Rare Forms of Hæmolytic Anæmia

Sickle-celled Anæmia.—This is a familial and hereditary disease found only in negroes. There is intermittent fever and severe hæmolytic anæmia, which ultimately proves fatal. Large numbers of the red cells are sickle-shaped. No treatment is effective.

Acute Hæmolytic Anæmia of Lederer.—Nothing is known of the ætiology of this rare condition, which usually occurs in adolescence. The onset is sudden and the degree of anæmia increases rapidly. The temperature is raised and hæmoglobinuria or slight jaundice may occur. There is often a leucocytosis with myelocytes or myeloblasts simulating acute leukæmia. Transfusion is often successful and this may help to differentiate the condition from leukæmia. Acute hæmolytic anæmia may very rarely follow the administration of sulphonamides.

Chronic Idiopathic Hæmolytic Anæmia.—This rare condition was in the past considered to be an acquired form of acholuric jaundice. It occurs in middle age and there is no family history. Although many of the features of acholuric jaundice, such as spherocytosis, increased fragility, and excess of reticulocytes may be present, they are more inconstant than in acholuric jaundice. The results of splenectomy are often poor.

PERNICIOUS ANÆMIA

(*Addison's Anæmia*)

Addison, in 1849, described by the term "idiopathic anæmia" a condition of profound anæmia occurring without any obvious loss of blood. This well-recognised clinical condition has since been generally known as pernicious anæmia. Its main incidence is between forty and seventy years of age and both sexes are equally affected.

Morbid Anatomy.—There is little evidence of emaciation. The skin is usually of a typical lemon-yellow tint (*vide* p. 268). The muscles are intensely red, while the subcutaneous fat is of a bright yellow colour. The heart is markedly flabby, with much fatty infiltration of the muscle; on naked-eye examination this is best seen beneath the endocardium covering the *musculi papillares* of the left ventricle, the condition being usually termed "tabby-cat striation." The liver is often large and fatty, with a colour exactly that of *café au lait*. With potassium ferrocyanide and hydrochloric acid the liver turns a Prussian-blue colour (*Perl's* test), due to an excess of iron-containing hæmosiderin. The spleen is enlarged in a majority of the cases. The bone marrow in the shafts of the long bones is deep red in colour, and a smear of the marrow shows numerous large nucleated red cells. The spinal cord appears normal on naked-eye inspection, but

histological examination may show the changes characteristic of subacute combined degeneration.

Pathology.—For normal maturation of the red cells in the bone marrow an anti-anæmic principle is necessary. To produce this it has been shown by Castle that two factors are required : (i) an intrinsic factor, which is produced by the gastric mucosa, especially that of the body and fundus of the stomach, at any rate in human beings. The intrinsic factor is thermolabile. (ii) An extrinsic factor, which is present in the protein of the food, especially in that of meat, or perhaps in the breakdown products of such proteins. The intrinsic and extrinsic factors are both necessary for the production of the " hæmopoietic or anti-anæmic principle " which, after it has been stored in the liver, is thermostable. This is formed by the interaction of the two factors and is absorbed from the small intestine into the blood, which carries it to the liver and other organs, where it is stored, particularly in the liver. Without the " hæmopoietic principle " the red cells in the bone marrow are incapable of normal maturation. In consequence of such impaired maturation, involving restricted division of some of the earliest forms, the circulating red cells are larger than normal, and the anæmia produced is macrocytic and hyperchromic.

Macrocytic anæmia may result from (i) absence or insufficiency of the intrinsic factor ; (ii) insufficiency of extrinsic factor ; (iii) inability of the intestine to absorb the anti-anæmic principle formed by the two factors ; (iv) a failure of the storage mechanism in the liver ; (v) a failure of the bone marrow to make effective use of the anti-anæmic principle.

By far the most frequent cause of macrocytic anæmia is the first, absence or insufficiency of the intrinsic factor, and this is the basis of the relatively common disease, pernicious anæmia.

As has already been stated, the intrinsic factor is evolved in the gastric mucosa. If the intrinsic factor is absent or deficient the supply of anti-anæmic principle to the marrow is rendered deficient. In the ætiology of pernicious anæmia it is necessary to determine how the supply of intrinsic factor comes to be defective. In pernicious anæmia it has been shown that almost without exception there is a gastric achylia, in which there is no secretion of free hydrochloric acid even after stimulation by histamine (*vide* p. 300). Such an achylia may result from a hereditary defect in the stomach. Thus it is found that not infrequently the disease is familial, and also that in a family where one member has pernicious anæmia others may show gastric achylia. Moreover, many patients who develop pernicious anæmia have been known to have been achylic for years before the anæmia develops. Nor does the achylia disappear during remissions of the anæmia, whether spontaneous or induced by liver treatment. It is clear, therefore, that the achylia which is such a constant feature of pernicious anæmia is not the result of the anæmia but is in some way related to its development. Yet there must be other factors necessary for the development of the disease besides achylia, for it is known that this anomaly is not uncommon, at any rate after middle-age, without producing symptoms of any kind. It is probable that the functions of the gastric mucosa are threefold, the secretion of hydrochloric acid, of enzymes, and of the intrinsic factor. It is clear, therefore, that an inability of the mucosa to produce acid or even enzymes, though this may constitute an achylia, is insufficient to cause pernicious anæmia unless the intrinsic factor is also absent.

Other factors apart from an inherent defect in the stomach may much more rarely produce achylia and pernicious anæmia. Thus surgical removal of a large portion of the stomach may occasionally be followed by pernicious anæmia. It may perhaps also result from damage to the mucosa by chronic gastritis or carcinoma.

Macrocytic anæmia may also result from a deficiency in the extrinsic factor. This may be the underlying cause in the so-called tropical anæmias, but it is doubtful whether it arises in non-tropical countries. A more frequent cause of macrocytic anæmia is failure of absorption of the anti-anæmic principle. This may occur with strictures of the intestine, usually tuberculous, or where abnormal anatomical conditions have arisen, such as a gastro-colic fistula. It is also likely to explain the macrocytic anæmia of sprue (*vide* p. 153), for in this disease absorption from the intestine is defective.

Storage of the anti-anæmic principle may be ineffective in widespread disease of the liver, such as cirrhosis, though in such cases the anæmia is seldom severe in relation to other features of the disease.

Anæmia similar in type to pernicious anæmia has been described by Wilkinson and Israëls which fails to react to liver and is not associated with achylia. The condition is termed *achrestic anæmia*. It is probably due to an inability of the hæmopoietic tissues to utilise hæmopoietin. The disease is rare and usually fatal.

Subacute combined degeneration of the cord is a frequent accompaniment of pernicious anæmia, and this condition may sometimes occur before anæmia becomes manifest. It is likely that the stomach secretes not only the intrinsic factor, which with the extrinsic factor produces the anti-anæmic substance, but also some other enzyme which is essential for the adequate nutrition of the nervous tissues. This hypothetical enzyme has been termed "neuropoietin."

Sepsis, such as infected tonsils or teeth, diminishes the effectiveness of liver in the treatment of pernicious anæmia. Possibly sepsis may in itself have a depressant effect on the hæmopoietic functions, tending to produce and maintain gastritis, or it may to some extent directly interfere with the absorption of the anti-anæmic substance.

While there is no true hæmolysis in pernicious anæmia, the van den Bergh test shows a positive indirect reaction. This is due to a failure of utilisation of the breakdown products of normal red cell destruction, and possibly the failure of excretion of these products owing to fatty changes in the liver.

Symptoms.—The symptoms and signs fall into two main groups: those resulting from the profound anæmia and resembling those found in other anæmias, and those which are more or less characteristic of pernicious anæmia. In the former group are such symptoms as dyspnœa, muscular weakness, headaches, palpitation, anginal pain, and œdema of the ankles, and among physical signs a systolic hæmic murmur in the pulmonary area. The onset of symptoms is remarkably slow and insidious. Many patients with pernicious anæmia remain at work until their hæmoglobin has fallen well below 50 per cent. The symptoms and signs characteristic of the disease are as follows:—

1. *Skin.*—When anæmia is severe there is a lemon-yellow tint, which, together with the positive indirect van den Bergh reaction, may disappear during remissions or with treatment.

2. *Gastro-intestinal Symptoms.*—The tongue is frequently red, smooth,

and devoid of papillæ, and the patient complains that it is very sore. Vague dyspeptic symptoms, often with diarrhœa, are not uncommon.

3. *Neurological Symptoms.*—Subacute combined degeneration of the cord is described on page 683.

4. *Spleen.*—This organ is palpable in less than half the cases, but it is never very large.

5. *Pyrexia.*—Most cases of untreated pernicious anæmia have a low, irregular pyrexia, which is often intermittent.

6. *Eyes.*—Retinal hæmorrhages occur in severe cases.

7. *The Blood Picture.*—The most characteristic feature of the blood is that the average size of the red cells is increased. Normal red cells average 7·2 μ in diameter, while in pernicious anæmia this figure may be as high as 9·4 μ. A similar blood picture is seen in other forms of macrocytic anæmia. These include pernicious anæmia of pregnancy, tropical nutritional anæmia, sprue, and the anæmia due to Dibothriocephalus. The increased mean diameter of the red cells explains the high colour index and raised mean corpuscular hæmoglobin content (*vide* p. 259) which are nearly always found in the disease. By the term colour index is meant the ratio between the hæmoglobin percentage and the percentage of the red cell count as compared with theoretical normals of 100 per cent. Hb (14·7 mg. Hb per 100 c.c. of blood) and 5,000,000 cells to the cubic millimetre (*vide* p. 259).

$$\text{C.I. (colour index)} = \frac{\text{Hæmoglobin percentage}}{\text{Red corpuscle percentage}}.$$

For example, with a red cell count of 1,000,000 and a hæmoglobin percentage of 25, the colour index $= \frac{25}{20} = 1{\cdot}25$, because 1,000,000 red cells represent 20 per cent. of the average normal count of 5,000,000. A colour index above unity indicates that the average diameter of the cells is above normal, while with a low colour index the cells may be of normal diameter with a diminished content of hæmoglobin (hypochromic) or may be actually smaller than normal (microcytic).

Although the *average* diameter of the red cells is high, there are also many abnormally small cells, and the variation in size is termed *anisocytosis*. The cells are also irregular or pointed in shape, a condition known as *poikilocytosis*. Basophil granules and "steel" blue staining of the cells occur, termed respectively *punctate basophilia* and *polychromasia*. During the later stages in the disease, many nucleated cells appear in the peripheral circulation; when of normal size these are described as *normoblasts*; but larger and extremely primitive forms, termed *megaloblasts* and *erythroblasts*, may finally appear. Megaloblasts are rarely seen except in advanced cases of pernicious anæmia, and are not necessarily found in every case.

The hæmoglobin percentage may fall to under 20 per cent. and the red cell count below 1,000,000, but even in earlier stages the nature of the anæmia is suggested by the megalocytosis, high colour index, and the positive indirect van den Bergh reaction.

The leucocyte count is always low except in the presence of a secondary infection, and seldom rises above 5,000 cells to the cubic millimetre. The differential count shows a diminution in the polymorphonuclear cells, with a relative increase in the lymphocytes. The polymorphs show a "shift to the right" (*vide* p. 258). The blood platelets are usually somewhat reduced.

Diagnosis.—In many cases a tentative diagnosis can be made on clinical grounds, but a careful blood examination and other investigations, including a test meal and a van den Bergh test, are important as confirmation. The disease with which pernicious anæmia is most likely to be confounded is carcinoma of the stomach. In the latter condition, however, the anæmia is usually of the microcytic type, with a low colour index, and although achlorhydria may be present there is often blood in the test meal, but in a few instances a pernicious type of anæmia has been known to develop. The presence of a palpable tumour, marked emaciation, and X-ray evidence will usually reveal the true diagnosis. The anæmia of sprue may exactly resemble that of pernicious anæmia, but the character of the stools and residence in the East will provide a clue. Severe anæmias resulting from loss of blood present a completely different clinical picture and rarely give rise to serious difficulty. In idiopathic hypochromic anæmia (*vide* p. 272) the blood picture is of the microcytic type and the condition reacts rapidly to treatment with iron.

Acute leukæmia may occasionally give a high colour index, but the character of the white cells makes the diagnosis clear. In obscure cases sternal puncture is of value.

The reaction of the anæmia to liver may be of diagnostic significance. If a patient thought to be suffering from pernicious anæmia does not respond to adequate liver treatment, the diagnosis must be reviewed.

Treatment.—It has already been stated that the administration of liver is a specific in pernicious anæmia. At the present time many extracts of liver suitable for intramuscular injection have been put on the market under trade names such as Anahæmin, Pernæmon, Examen, and Hepatex. The dosage of such preparations varies with the concentration of the particular extract, and they have entirely replaced the oral administration both of liver or liver extract. It has been found, however, that these highly purified extracts are often less efficacious than the cruder preparations of liver when used in the treatment of other megalocytic anæmias, such as tropical nutritional anæmia. When a megalocytic anæmia fails to respond to parenteral liver, proteolysed liver should be given by mouth. This is often most effective in so-called refractory megalocytic anæmia. Folic acid produces a reticulocyte response and an increase in hæmoglobin and red cells in most macrocytic anæmias.

Intramuscular injections have many advantages over oral administration ; firstly, they are very much cheaper than adequate amounts of liver given orally. Secondly, patients readily tire of eating liver and consequently may omit to do so, a course which inevitably leads to relapse. Intravenous injection is usually both unnecessary and dangerous. A few instances of acquired hypersensitivity to liver extract injections have been recorded ; they may be controlled by coincident injection of adrenalin or may disappear if the type of extract is changed.

Injections of liver extract should be started as soon as a diagnosis of pernicious anæmia is made. If the preparation used is a potent one, such as Anahæmin (B.D.H.) or Examen (Glaxo), 2 to 4 c.c. weekly is often sufficient to produce a satisfactory response, but as larger amounts of extract are not harmful it is perhaps safer in severely anæmic patients to give injections on alternate days in the earlier weeks of treatment.

Striking changes in the blood occur with the institution of liver treatment,

and the more anæmic the patient the more effective is the liver. The first indication that liver is producing an effect is the appearance of an increased number of reticulocytes in the blood. In the untreated patient with pernicious anæmia, reticulocytes (*vide* p. 257) seldom exceed 1 to 3 per cent. of the red cells. Within five days or less of starting treatment the number of reticulocytes increases, and by between the fifth and tenth day they have usually risen to between 15 and 40 per cent. Concurrently with the increase of reticulocytes, or as it is often called a reticulocyte response, there is a rise in the percentage of hæmoglobin and in the red cell count. After about the tenth day or earlier the reticulocytes begin to diminish in number, and after some weeks have returned to their normal figure. The hæmoglobin and red count, on the other hand, continue to rise, and within about eight to ten weeks may have reached normal figures. During liver treatment the leucocyte count rises. The red cells become normal in size and shape and the colour index approximates to unity.

With the changes in the blood there is a rapid improvement in the condition of the patient. The lemon-yellow tint of the skin disappears and the indirect van den Bergh test becomes negative. Weakness, breathlessness, and depression are replaced by a feeling of well-being and the appetite increases. Subjective symptoms due to subacute combined degeneration, such as numbness and tingling in fingers and toes, disappear, but when there are objective symptoms of structural nervous disease, such as extensor plantar responses, these are little affected by liver treatment, though there may be a remarkable improvement in the clinical condition (*vide* p. 686).

Even though the patient may improve rapidly under the influence of liver, it is essential to insist upon adequate rest in bed, which should be maintained until the hæmoglobin reaches 70 per cent. As soon as he is sufficiently fit, any infective foci, such as teeth or tonsils, should be dealt with.

Blood transfusion is now very rarely necessary in pernicious anæmias and should only be employed if the patient is *in extremis*, or, with fresh blood, as an initial stimulus to patients failing to respond to the usual treatment.

Desiccated stomach (*e.g.*, Pepsac, Ventriculin) may be given in addition to liver. This is given by mouth in doses up to 1 oz. a day, and is said to be of special value in the treatment of subacute combined degeneration.

Iron has no specific effect on pernicious anæmia, but when the anæmia is severe it should be given (*vide* p. 272). Plenty of fresh air, sunshine, and a liberal mixed diet of adequate vitamin content should be ensured.

Prognosis.—In the past, pernicious anæmia justified its sinister name and was almost invariably fatal within a few years, though usually there were several remissions, either spontaneous or induced by transfusions. With liver treatment, carried out conscientiously, the outlook has entirely changed, and patients live an active and useful life for an indefinite period.

It is most important to keep the patient under close supervision and control until the hæmoglobin and red cell count reach normal figures. After discharge from hospital a maintenance dose of liver extract must be given at regular intervals, at first fortnightly. Later a monthly injection is often sufficient. A blood count should be done monthly for three months and then three-monthly for the rest of the patient's life. It is essential to impress on the patient that if he omits the injections relapse is inevitable. Curiously

enough a hæmatological relapse may precede any symptoms for many months —hence the importance of routine blood counts.

Idiopathic Hypochromic Anæmia

Ætiology.—Idiopathic hypochromic anæmia, sometimes described as Simple Achlorhydric Anæmia, is so called because the corpuscles contain less hæmoglobin than normal. It is the result of a deficiency of iron, either owing to lack of iron in the diet or more often to imperfect absorption of the metal. Menorrhagia, pregnancy, and lactation often play a part in its production. Achlorhydria, or extreme hypochlorhydria, is an almost constant finding, and it is probably owing to this that absorption of iron is defective. The condition is sometimes familial and examples of pernicious anæmia and idiopathic hypochromic anæmia may be found in a single family. Probably the explanation of this fact lies in an inherited tendency to achlorhydria or gastritis in certain families. The condition, though often unrecognised, is very common and a frequent cause of chronic ill-health in middle-aged women.

Symptoms.—These will depend on the degree of anæmia, and include lassitude, breathlessness, palpitation, vague dyspepsia, anorexia, and pallor, which, however, even when severe has not the yellow tinge of pernicious anæmia. The nails are often atrophic and spoon-shaped (koilonychia). The tongue may be smooth and atrophic and cracks may occur at the corners of the mouth (perlèche). The spleen is sometimes slightly enlarged.

The patient sometimes complains of a difficulty in swallowing localised to the lower pharyngeal region. This results from a chronic hypopharyngitis, sometimes precancerous, which produces a definite narrowing of the lumen of the pharynx. There may be a failure of relaxation of the sphincter formed by the lower division of the inferior constrictor muscle of the pharynx, analogous to that which occurs in achalasia of the cardia. Dysphagia of this type in anæmia is often described as the Plummer-Vinson syndrome. It can be relieved by passing a thick rubber mercury bougie, and it disappears when the anæmia is abolished by treatment with iron.

The blood count is not characteristic, but the red cells are usually smaller than normal and the colour index is always low, usually about 0·6 to 0·7, as are also the mean corpuscular hæmoglobin and the mean corpuscular volume. The average red count is 3 to 4 millions and the hæmoglobin 40 to 50 per cent. The leucocyte count is normal. There is no hæmolysis and the van den Bergh reaction is negative.

The condition is an extremely chronic one and patients have often been known to have suffered from anæmia for years before a definite diagnosis is made.

Diagnosis.—Idiopathic hypochromic anæmia must be differentiated from anæmia due to other causes, such as carcinoma or chronic hæmorrhage. A careful clinical examination and investigations are important to exclude such causes for the anæmia.

Treatment.—Iron, provided it is given in sufficiently large doses, is as specific in the treatment of idiopathic hypochromic anæmia as is liver in pernicious anæmia. It must be given in doses at least twice as large as the maximal pharmacopœial dose, and should always be given by mouth. Suitable preparations are iron and ammonium citrate, of which at least

90 gr. should be given in the twenty-four hours. The drug is best given as a saturated solution in 20 to 30 minim doses thrice daily taken in a small quantity of milk. This masks the astringent taste. Blaud's pill (Pilula Ferri B.P.) is an alternative. The pills must be fresh and three or four of the 5 gr. pills should be taken crushed thrice daily. Ferrous sulphate preparations, such as Fersolate (Glaxo), are palatable and non-constipating. Relapse is not infrequent and routine blood counts should be done three-monthly. If these show any indication of recurrence of anæmia, iron should be given at once.

Chlorosis.—This form of anæmia was extremely common until thirty years ago among adolescent females, but it is now never seen, probably as a result of improved conditions of life. It was characterised by an anæmia with low colour index and a greenish tint of the skin. It was often associated with digestive disturbances and hyperchlorhydria. Like idiopathic hypochromic anæmia, chlorosis responded readily to iron.

Aplastic Anæmia

In this rare form of anæmia there is a failure on the part of the bone marrow to produce, properly formed, the elements of the blood, including red cells, white cells, and platelets. The erythropoietic tissue is chiefly involved. Aplastic anæmia may result from the effects of certain poisons on the bone marrow, such as benzol, occasionally arsphenamine, sulphonamides, radium, X-rays, and thorium. Some cases are met with in which there is no obvious cause. The bone marrow is fatty and atrophic.

The symptoms are those of a profound anæmia; the colour index is usually about unity, the red cells of normal average diameter (normocytic), and the white count is low. The platelets may be also much diminished, in which case hæmorrhages and petechiæ are a prominent feature, as in thrombocytopenic purpura. Progress is nearly always steadily downhill, and liver and iron produce no beneficial effects. Blood transfusion with "packed cells" (*vide* p. 264) is of temporary benefit, but usually within a few weeks the anæmia becomes as severe as ever. A few patients have been kept alive for several years by transfusions at about fortnightly intervals. Owing to the very low white count and inability to produce a physiological leucocytosis, patients with aplastic anæmia have very poor resistance to infections.

Leukæmia, multiple myelomatosis, osteosclerosis, and multiple secondary carcinomatous deposits in bone may produce an anæmia of aplastic type. Immature red and white cells may be present, and the condition has been termed leuco-erythroblastic anæmia. Chronic sepsis or nephritis may markedly inhibit erythropoiesis. Similar effects may be seen in lack of vitamin C (scurvy) and thyroxin deficiency (myxœdema).

Anæmia in Pregnancy

Since the war anæmia during the later months of pregnancy has attracted considerable attention. Three types have been recognised: (i) microcytic iron-deficiency anæmia; (ii) megalocytic anæmia of pernicious type; (iii) hæmolytic or "refractory" anæmia.

The microcytic type is seldom severe but is relatively common, especially

among the hospital class of patient. It can be prevented or cured by giving iron. It probably is due to war-time dietary.

The macrocytic type has a blood picture similar to that of pernicious anæmia, but gastric achylia is not a constant finding, though the gastric acidity is often low. The anæmia is often severe. The condition appears to be common in India but relatively infrequent in Great Britain. Most of the patients react readily to liver treatment, but in specially severe cases blood transfusion may be required in addition. After parturition, continuance of liver treatment is unnecessary.

The hæmolytic or "refractory" type is relatively rare. The anæmia is megalocytic but the patient is usually refractory to liver extracts given by injection. The percentage of reticulocytes is high even before liver is given and there is a strongly positive indirect van den Bergh reaction. Blood transfusions are effective. This type of anæmia often responds to proteolysed liver taken by mouth.

Agranulocytosis

The term agranulocytosis indicates a condition in which there is an absence of, or a great diminution in, the granular forms of leucocytes. The total white cell count is low and the polymorphonuclear cells may be reduced to 5 per cent. or less. In conjunction with this agranulocytosis the patient suffers from severe ulcerative and necrotic inflammation, most commonly seen around the fauces and buccal cavity, but sometimes in other regions, such as the rectum or vagina. The onset of symptoms is usually sudden, though the patient may have been in poor health for some time. The temperature is raised and the constitutional symptoms severe. Death often occurs within a week. In view of the frequency of ulceration in the throat, the condition is sometimes described as agranulocytic angina.

The agranulocytosis probably precedes the necrotic lesions, which occur as a result of secondary infection owing to the patient's diminished powers of resistance. The absence of granular white cells in the blood may be due to interference with the maturation of the precursors of the granular leucocytes in the bone marrow. The factors which influence the bone marrow are unknown, but in a large proportion of cases of agranulocytosis drugs appear to be the chief ætiological factors. The condition may follow the taking of amidopyrine (pyramidon) or preparations which contain amidopyrine. The sulphonamide group of drugs may cause agranulocytosis (*vide* p. 7). Agranulocytosis occasionally occurs after administration of arsphenamine, gold, and thiouracil. In recent years the condition has become much more common, possibly due to widespread use of sulphonamides.

Agranulocytosis develops, though very rarely, in overwhelming infections, such as septicæmia. More often it complicates aplastic anæmia or aleukæmic leukæmia. Its differentiation from the latter condition may only be possible by sternal biopsy.

The mortality of agranulocytosis is high, probably between 40 and 80 per cent. Transfusion of fresh blood may be used as a temporary measure. Stimulating doses of X-rays to the long bones have sometimes produced a rise in the granular elements of the blood and a remission of symptoms. Perhaps more valuable is Pentnucleotide, which stimulates the bone marrow to produce granulocytes. The drug is available in 10 c.c. ampoules, each

containing 0·7 gm. One ampoule is injected intramuscularly four times a day until the leucocyte count begins to rise ; this may be expected to occur in four or five days. Subsequently two ampoules a day are given until the count reaches normal figures. Penicillin should be given, as some of the organisms in the throat may be sensitive to this drug.

Needless to say, in every case of agranulocytosis it is essential to ascertain that the patient is not taking on his own account any of the drugs which might give rise to the disease.

PURPURA

There are many conditions in which hæmorrhage may occur in the skin, from the mucous membranes, in the joints, or indeed in any organ of the body. At the present time our knowledge of the pathology of such hæmorrhagic states is very incomplete, and it is therefore difficult to draw up any satisfactory classification on an ætiological basis. The following provisional classification is based chiefly on clinical experience :—

1. Symptomatic purpura. This may occur in infections, *e.g.*, septicæmia, subacute bacterial endocarditis, cerebrospinal fever, and the hæmorrhagic forms of the specific fevers. It also occurs in toxic conditions, *e.g.*, uræmia, cirrhosis of the liver, and in severe anæmias and leukæmias.

2. Purpura hæmorrhagica (thrombocytopenic purpura).

3. Hereditary hæmorrhagic states : (i) hæmophilia ; (ii) hereditary telangiectasia ; (iii) hereditary purpura hæmorrhagica.

4. Anaphylactoid purpura : Henoch's and Schönlein's purpura.

Hæmorrhage may obviously result from a number of factors, concerned either with the blood itself or some alteration in the permeability of the capillaries. It is not necessarily in association with failure of the blood to clot. Indeed, in most forms of hæmorrhage, except in hæmophilia, there is no prolongation of the clotting time. Diminution in the number of platelets may be associated with a tendency to hæmorrhage, and in the severe form of purpura, often known as thrombocytopenic, the platelets may be practically absent. Hæmorrhage of the purpuric type is, however, not necessarily associated with a decrease in the number of platelets. Thus in anaphylactoid purpura the fault is probably an increased permeability of the capillary wall, and the condition may be allied to urticaria. The underlying cause of thrombocytopenia (diminution in the number of platelets) is as yet uncertain.

Symptomatic Purpura

Little is known of the pathological changes associated with symptomatic purpura. The platelets may be decreased, normal, or increased in number. Probably the purpura is due to changes in the walls of the capillaries, induced perhaps by infection or toxæmia. The variations in the platelet content of the blood may be purely a secondary result of the hæmorrhage. Symptomatic purpura may occur in the following conditions :—

1. *Infections.*—Most of the specific fevers, such as measles and smallpox, have hæmorrhagic forms, fortunately rare, in which hæmorrhage occurs in the skin and elsewhere. In cerebrospinal fever cutaneous hæmorrhages are relatively common and have given the disease its name of spotted fever.

Purpura in the form of petechiæ and ecchymoses is common in streptococcal and staphylococcal septicæmia. It also occurs in subacute bacterial endocarditis, where it may be the result of minute infarcts.

2. *Toxic Disturbances.*—Purpura may be present in uræmia, cirrhosis of the liver, and in advanced malignant disease.

3. Numerous drugs may produce purpura in persons who are in some way sensitive; these drugs include copaiba, quinine, iodine, gold, arsphenamine, and "Sedormid."

4. *Severe Anæmia.*—In severe anæmia of all types cutaneous hæmorrhage is not uncommon. This is specially true of the acute leukæmias, aplastic anæmia, and pernicious anæmia, in all of which the platelets may be greatly diminished in number.

5. *Vitamin Deficiencies.*—Scurvy, both adult and infantile.

Thrombocytopenic Purpura

This condition is also termed Purpura Hæmorrhagica or Essential Thrombocytopenia, owing to the fact that the platelets are much diminished in numbers. It varies very greatly in its degree of severity. It is probable that the disease is due to a failure of maturation of the platelets, comparable to the failure of erythrocyte maturation in pernicious anæmia. Some inhibitory factor may be produced by the spleen, as splenectomy usually cures the disease. The coagulation time of blood collected in a tube is normal, *i.e.*, about three and a half to four minutes at 37° C., but the bleeding time (*vide* p. 258) is much prolonged, if at the time it is tested the patient is suffering from hæmorrhage. Normally the bleeding from a simple prick should cease within about three to four minutes. In thrombocytopenic purpura it may be sometimes observed to continue four or five times as long.

Symptoms.—Thrombocytopenic purpura occurs both in an acute and chronic form. In the former the onset may be very abrupt with profuse hæmorrhage, which renders the patient dangerously anæmic within a few hours. The bleeding may be from a number of different areas, such as the nose, intestinal tract, or uterus, or it may be at first entirely from a single source. There are, however, nearly always some petechiæ or ecchymoses in the skin, which point to the condition being a general rather than a local one. In some cases bleeding may persist whatever is done, and the patient may die within a week of anæmia, and exhaustion, or a cerebral hæmorrhage may prove fatal. More often, however, the bleeding ceases and within a few weeks the patient is restored to comparatively good health. Recurrences of hæmorrhage, however, are common.

Chronic forms of thrombocytopenic purpura, which often start in childhood, are more frequently encountered. Purpura is recurrent or persistent and hæmorrhage occurs from the mucous membranes, but it is usually not so severe as in the acute forms and the patient is less anæmic. In chronic types the spleen is often palpable, whereas in the acute type there is seldom any obvious enlargement.

In all forms of thrombocytopenic purpura the platelet count is low when the patient is having symptoms, but during remissions it may reach a normal figure (250,000 to 400,000 per c.mm.). When the platelets fall below 40,000, hæmorrhage usually occurs, and during severe bleeding the platelets may be almost completely absent. There is generally a slight leucocytosis,

and nucleated red cells may be seen. The so-called "capillary resistance" test is positive when bleeding is likely to occur. The tourniquet of a blood-pressure apparatus is put around the arm and blown up to midway between the diastolic and the systolic pressures for five minutes. The cuff is then removed, and if the test is positive, numerous purpuric spots appear below the level of the tourniquet. If blood is drawn from a patient with active thrombocytopenic purpura the retraction of the clot is delayed, though there is no prolongation of clotting time.

Differential Diagnosis.—Acute thrombocytopenic purpura can be readily distinguished from acute leukæmia by the presence of myelocytes and myeloblasts in the latter disease; in acute leukæmia and aleukæmic leukæmia, as in thrombocytopenic purpura, the platelets may be very much reduced. It is important to remember that sometimes purpura may be almost or completely absent, and if the bleeding is always from one organ, such as the intestine, there is a risk of the general nature of the disease being overlooked. In such cases the platelet count is of great value, as is also a sternal biopsy. The symptomatic purpuras are usually readily distinguished if the patient is thoroughly examined.

Treatment.—In many of the milder cases rest in bed abolishes the symptoms, and in the chronic forms of the disease, as the patient gets older the condition abates. No drugs (including liver) are of any value, though iron may aid convalescence when hæmorrhage has ceased. In chronic types splenectomy often produces remarkably successful results, and provided the patient is not seriously anæmic at the time of operation the mortality is low. In the acute forms of the disease with severe hæmorrhage the mortality of splenectomy is very high, and before contemplating operation there should be adequate slow transfusion of fresh blood. Hæmorrhage sometimes ceases abruptly following transfusion of a pint of fresh blood. The platelet count rises immediately after transfusion, and later usually falls again to below normal, but immediate recurrence of symptoms is unusual. Splenectomy should only be advised when the diagnosis of thrombocytopenic purpura has been confirmed by recurrent hæmorrhage, a low platelet count, prolonged bleeding time and a normal coagulation time, and a positive capillary resistance test.

Hereditary Hæmorrhagic States

1. **Hæmophilia.**—This remarkable hereditary disease is confined to males, but is transmitted by the female, who, however, shows no manifestations of it herself. Family records show the persistence of the condition over periods as long as two hundred years. The clotting time of the blood is unduly long. This is probably due to increased stability of the platelets, whereby they do not disintegrate and liberate the thrombokinase required for the activation of prothrombin. The bleeding time in hæmophilia is normal.

Symptoms commence in infancy and are usually most severe before puberty; in those who survive to adult life the tendency to hæmorrhage diminishes. Bleeding may occur into the skin in the form of ecchymoses, as the result of minor degrees of trauma. Hæmorrhage from the mucous membranes, particularly from the nose and gums, is common. Small cuts may bleed steadily for hours as the result of capillary oozing, and even

minor operations such as the extraction of teeth may be fatal. When bleeding is prolonged severe anæmia may develop, but the blood-forming organs appear to have great powers of blood regeneration. Occasionally hæmorrhages occur into joints, which become swollen and painful. Splinting and aspiration are often effective but a crippling osteoarthritis may result.

Various measures have been tried for stopping bleeding; if the site is readily accessible, firm and prolonged pressure may be effective. Adrenalin or snake venom may be applied locally, and direct applications and injections of normal horse serum are recommended. Blood transfusion with fresh blood helps to promote coagulation as well as to restore hæmoglobin to the circulation, and is essential immediately before even the smallest surgical procedure. Trauma must be avoided at all costs and operations or tooth extraction performed only when absolutely necessary. Females from a hæmophilic family should not bear children.

2. **Hereditary Telangiectasia.**—In this rare condition, minute telangiectases or angiomata are found on the skin and mucous membranes, particularly in the nose. The cutaneous telangiectases are innocuous, but those in the nose or alimentary canal may bleed and produce severe anæmia. The condition is hereditary and familial, affecting both sexes. Iron and transfusions are the only treatment available.

3. **Hereditary Purpura Hæmorrhagica.**—In certain families there is a tendency to hæmorrhage, as shown by epistaxis or purpura. The coagulation time is not lengthened but the platelets are generally low and the disease resembles thrombocytopenic purpura. Splenectomy is of no value, and if severe hæmorrhage occurs transfusion may be necessary.

Anaphylactoid Purpura

This type of purpura includes Henoch's purpura and Schönlein's disease. There is neither deficiency of platelets nor lengthening of the coagulation time. The walls of the capillaries are unduly permeable and allow blood cells and plasma to pass out into the tissues.

In Schönlein's disease purpuric spots, urticarial wheals, or angioneurotic swellings appear on the skin, and joints may be swollen and tender. There is often slight pyrexia and a sore throat. The condition was formerly thought to be akin to acute rheumatism and was known as peliosis or purpura rheumatica. Spontaneous recovery takes place without treatment.

In Henoch's purpura the main symptoms are attacks of severe abdominal pain, vomiting, and diarrhœa. Blood may be passed by the bowel. Swelling of joints, purpura, and urticaria occur, but are a less prominent feature than in Schönlein's disease. The abdominal symptoms are due to exudation of plasma and blood into the wall of the intestine. Rarely this may produce an intussusception. Treatment is symptomatic only, and on no account should splenectomy be performed. Anaphylactoid purpura occurs mainly in children and during early adult life.

LEUKÆMIA

Under the general heading of leukæmia are included a number of clinical conditions in which the white cells are abnormal, both quantitatively and

qualitatively. While the various forms of leukæmia differ widely in their symptoms and course, they resemble one another in that they are eventually uniformly fatal.

The leukæmias are classified into acute and chronic varieties and also according to the type of leucocyte chiefly involved. The acute leukæmias comprise acute myelogenous and acute lymphatic, according as the neutrophils or the lymphocytes are at fault. The chronic types consist of chronic myelogenous (often termed spleno-medullary) leukæmia, which is very occasionally eosinophilic, and chronic lymphatic leukæmia. In addition, there are rare forms of leukæmia known as aleukæmic leukæmia (*vide* p. 280), chloroma, monocytic leukæmia, and leuco-erythroblastic anæmia. The acute leukæmias are difficult to distinguish on clinical grounds and may be described together.

Nothing is known of the ætiology of the leukæmias. By some they are regarded as new growths of the bone marrow, by others as a reaction of the marrow to infection. Occasionally acute leukæmia has followed injuries of bones or osteomyelitis. Heredity does not appear to play any part.

Acute Leukæmia.—The main clinical features of the acute leukæmias are a rapidly fatal illness, pyrexia, a liability to early and severe hæmorrhage, ulcerative and necrotic lesions in the mouth, and a severe and rapidly progressive anæmia usually of a microcytic type. Primitive red cells of all types, particularly normoblasts and reticulocytes, are frequently present. The spleen and lymphatic glands are seldom much enlarged and often impalpable. The blood picture varies with the acuteness of the disease and the type of white cell mainly implicated. The total leucocyte count is rarely over 30,000 until shortly before death, when it may rise suddenly to 100,000. Acute myelogenous leukæmia is the type most commonly encountered; in this disease practically all the circulating white cells are myeloblasts. By ordinary staining methods the myeloblasts are non-granular and may be confused with large lymphocytes, but they may be shown to be primitive forms of granular cells if stained by the peroxidase method, which stains the granules in the cytoplasm of all but the most immature cells of the granular series. In acute lymphatic leukæmia, which is excessively rare, the lymphocytes and lymphoblasts account for over 90 per cent. of the total white count.

The onset of acute leukæmia is usually abrupt and resembles that of any acute pyrexial illness. Very rarely the white cells may at first show no very definite abnormalities. In some cases severe ulceration and necrosis of the gums, tonsils, and pharynx are striking features and are really due to agranulocytosis (*vide* p. 274). In others, hæmorrhagic symptoms predominate, such as epistaxis, uterine hæmorrhage, purpura, hæmorrhage into the brain or retina or from the intestinal or urinary tract. The hæmoglobin rapidly falls to about 20 per cent. and the colour index is usually low. Occasionally lymphoid deposits are found in the skin. Patients with acute leukæmia seldom survive for more than a few months, and in the more acute varieties death may occur within a fortnight.

Chronic Myelogenous Leukæmia. — The onset is extremely insidious and often the first symptom is a sensation of dragging or weight in the left side of the abdomen due to an enormously enlarged spleen. The patient may also complain of lassitude and general ill-health. Sometimes a retinal hæmorrhage may lead to the discovery of the condition. Blood examination

in the early stages may show counts up to several hundred thousand leucocytes per cubic millimetre, but the hæmoglobin percentage and the number of red cells are often but little reduced. A typical differential count in a relatively early case shows the following percentages : neutrophils, 70 per cent. ; eosinophils, 2 per cent. ; basophils, 3 per cent. ; myeloblasts, 2 per cent. ; myelocytes, 18 per cent. ; lymphocytes, 4 per cent. ; hyalines, 1 per cent. Basophil leucocytes are usually rather numerous, and this increase may call attention to the abnormal blood picture in early cases. Normoblasts often occur and increase in number as the leukæmia progresses. On physical examination the spleen is enormously enlarged and may extend down to the left iliac fossa, and its sharp edge with well-marked notches extends beyond the umbilicus. No glands are palpable, and the liver is usually not enlarged.

In the course of months, or even years, anæmia of a hypochromic type develops and the general health becomes increasingly impaired. The blood picture may change to that of acute myelogenous leukæmia, and the percentage of myeloblasts steadily increases. At this stage there may be hæmorrhage from mucous membranes. Ultimately death occurs from exhaustion or intercurrent infection. Pyrexia is absent until severe anæmia develops. In a very rare form of the disease all the immature cells are found to be eosinophilic (eosinophilic leukæmia).

Chronic Lymphatic Leukæmia.—This type is relatively rare and usually occurs in males above the age of fifty. The onset is gradual, and the most striking clinical features are a generalised enlargement of the lymphatic glands, which are discrete and painless. The spleen is easily palpable but does not reach the enormous size attained in myelogenous leukæmia. The liver is often enlarged. The total white count is rarely over 100,000 and at least 90 per cent. of the cells are small lymphocytes with occasional lymphoblasts. Gradually a microcytic anæmia develops. Sometimes after a number of years an acute leukæmia may occur, or the patients die of exhaustion or from secondary infection.

Aleukæmic Leukæmia.—Rarely in leukæmia the total number of white cells may remain low, but a differential count usually shows a high proportion of immature forms, *i.e.*, myeloblasts, myelocytes, or lymphoblasts. Sometimes the total white count may even be under 1,000. Most of the patients of this type ultimately develop obvious leukæmia, the white count rising considerably shortly before the end. If the leukæmic changes in the blood are not obvious the disease may be mistaken for aplastic, pernicious anæmia, or agranulocytosis. A sternal biopsy will usually settle the diagnosis.

Chloroma.—In this very rare condition nodular growths of lymphoid tissue are formed under the periosteum, especially in the orbit, skull, long bones, and sternum. The blood count is that of acute leukæmia. Death occurs early, and a section of the chloromatous tumours shows a green colour which rapidly fades on exposure to air.

Monocytic Leukæmia.—This condition is rare and tends to occur in middle life. It is frequently associated with ulcerative conditions in the mouth and pharynx, and is usually fatal within a few months. In it the total white count is as a rule less than 50,000, and 50 to 90 per cent. of the white cells are monocytes.

Differential Diagnosis of the Leukæmias.—Careful examination of even a single blood film usually provides sufficient evidence for a diagnosis of

leukæmia, and in the case of the acute forms of the disease it is often difficult, if not impossible, to arrive at a correct diagnosis without the aid of a microscope. Failure to diagnose acute leukæmia is almost invariably due to lack of this elementary precaution. In every case of purpura or hæmorrhagic manifestations, unexplained severe anæmia, continued fever or ulcerative stomatitis, the suspicion of leukæmia must be borne in mind and a careful blood examination made. In the acute leukæmias, especially when hæmorrhage is occurring, the platelets are diminished in number as in thrombocytopenic purpura. A differential leucocyte count, however, will usually settle the diagnosis between leukæmia and purpura.

With the chronic forms of leukæmia there is rarely any difficulty in diagnosis. In the myelogenous form the disease can often be diagnosed with fair certainty on clinical grounds alone, and a blood examination will settle any confusion with splenic anæmia or acholuric jaundice. Chronic lymphatic leukæmia may be mistaken for Hodgkin's disease, lymphosarcoma, glandular tuberculosis, or glandular fever unless the blood is examined.

Prognosis and Treatment of the Leukæmias.—As has already been stated, acute leukæmia in all its forms is rapidly and invariably fatal, and symptomatic treatment only is available. Blood transfusion is of doubtful value and may produce severe reactions. In chronic myelogenous leukæmia deep X-ray therapy to the spleen and long bones undoubtedly reduces a high leucocyte count and the size of the spleen and makes the patient more comfortable. As the disease progresses, X-ray treatment loses its efficacy, and it is doubtful whether it appreciably delays the ultimate fatal issue. It does, however, keep the patient relatively fit for a longer time. In chronic lymphatic leukæmia deep X-ray treatment to the enlarged glands diminishes their size.

The course of all chronic leukæmias is variable in individual cases. Patients have been known to live, even without treatment, for ten years or more, but most die within three years. Sometimes a subacute variety of myelogenous leukæmia is encountered in which deep therapy is of little avail, and the patient dies within twelve months.

POLYCYTHÆMIA

Polycythæmia is a condition in which the number of red corpuscles is increased. Sometimes the increase is only relative, as, for instance, when the loss of large quantities of fluid from the body produces a concentration of the blood ; in others there may be an absolute increase in the number of corpuscles, as, for example, in congenital heart disease or in those who reside at high altitudes. Apart, however, from conditions leading to a secondary polycythæmia, there may be a persistent and real increase in the red corpuscles. Such cases are known as polycythæmia vera or erythræmia.

Erythræmia.—Nothing is known as to the causation of the condition, which occurs mainly in later life and is associated with a moderate enlargement of the spleen and sometimes with some degree of hypertension. The appearance of the patient is fairly characteristic. The colour of the skin is bluish-red rather than dark blue, as in cyanosis or congenital heart disease, and dilated veins may be visible. Complaint is made of headache, lassitude,

and breathlessness. The red count varies from about 6,000,000 to 10,000,000 cells per cubic millimetre, and the leucocyte count is usually high. The hæmoglobin is well above 100 per cent., but the red cells are usually increased out of proportion to the hæmoglobin percentage. The heart is often dilated. Occasionally patients with erythræmia ultimately develop leukæmia.

The disease is a chronic one, which may last for years, with exacerbations and remissions, and the patient may die of intercurrent infection or sometimes as the result of cerebral hæmorrhage or thrombosis. Large hæmorrhages may occur from the alimentary tract, nose, or elsewhere, rendering the patient anæmic. Some patients show a tendency to intravascular clotting with its resultant sequelæ, such as coronary thrombosis. Repeated venesections help to relieve the symptoms, and X-ray applications to the long bones are often successful. The administration of phenylhydrazine hydrochloride reduces the red cell count by increasing the tendency to hæmolysis, but it must be given with caution as the effect may be prolonged and the fall in the red count continue after administration of the drug has ceased. This is given by mouth in capsules containing 2 gr. for seven to ten days, but its use must be carefully controlled by red and white cell counts. Acetylphenylhydrazine is said to be equally effective and less toxic.

Methæmoglobinæmia and Sulphæmoglobinæmia

In these conditions the most striking clinical feature is cyanosis, affecting chiefly the lips, mucous membrane of the mouth and the nail-beds, unaccompanied by any respiratory embarrassment. The cyanosis is due to the formation of methæmoglobin or sulphæmoglobin in the blood. In the great majority of cases the cyanosis is due to sulphæmoglobin, and occurs as a result of repeated ingestion of certain aniline dye derivatives, such as acetanilide or phenacetin ; these drugs are often present in " headache " remedies. Sulphanilamide also produces cyanosis (*vide* p. 6). Probably other factors apart from such drugs may play a part in the production of cyanosis. Most of the recorded cases of sulphæmoglobinæmia give a history of severe and chronic constipation, and it is probable that hydrogen sulphide formed in the colon may, under the influence of the aniline derivatives, unite with hæmoglobin to form sulphæmoglobin. In addition to constipation there is often a history of frequent headaches and some degree of mental instability, the headache being generally the reason for the drug habit. Methæmoglobinæmia is a rarer condition, and occurs as an acute poisoning following a massive dose of aniline derivative, either ingested or absorbed through the skin. The condition has also been described in a few patients in whom there appeared to be no evidence of drug addiction.

The disease is readily diagnosed by the discovery of the absorption bands of methæmoglobin or sulphæmoglobin in the blood spectrum. Clinically it may be suspected when cyanosis, particularly affecting the lips and fingers, occurs without any history or evidence of shortness of breath on exertion. With withdrawal of the drug concerned the cyanosis rapidly disappears if it is due to methæmoglobin, but much more slowly in cases of sulphæmoglobin. No special treatment is usually required beyond keeping the bowels open. Sulphates must not be given for this purpose.

Hæmoglobinæmia and Hæmoglobinuria

In normal blood hæmoglobin is present in the corpuscles only, but in a variety of pathological conditions it is found also in the plasma owing to disintegration of red corpuscles. When this occurs hæmoglobin is excreted in the urine and the patient is said to be suffering from hæmoglobinuria. The occurrence of the latter symptom always implies the existence of hæmoglobinæmia or free hæmoglobin in the plasma.

Hæmoglobinæmia occurs in the following conditions: (i) following blood transfusion if the serum of the recipient hæmolyses the donor's corpuscles; (ii) in blackwater fever (*vide* p. 140); (iii) in poisoning by certain drugs, notably potassium chlorate and arseniuretted hydrogen; (iv) in severe burns. In addition to the above, hæmoglobinæmia and hæmoglobinuria occur as transient but recurring phenomena in certain individuals, who are then said to suffer from paroxysmal hæmoglobinuria.

Paroxysmal Hæmoglobinuria.—The paroxysms are initiated by exposure to cold. During attacks there may be general symptoms such as lassitude, vomiting, and slight pyrexia. The urine becomes dark in colour, and on spectroscopic examination shows the absorption bands of hæmoglobin and often of methæmoglobin, but no red corpuscles can be seen with the microscope. Attacks last from a few hours to a day and are seldom dangerous to life, but occasionally the deposition of hæmoglobin in the renal tubules leads to anuria and uræmia.

If the finger of a patient liable to hæmoglobinuria is placed in iced water with its circulation stopped by a tourniquet, within a few minutes hæmoglobinæmia occurs, and blood taken from the finger contains free hæmoglobin in the plasma. Also, if the serum of the patient be mixed with normal red corpuscles and cooled, the latter become laked. Both these experiments indicate that cold is the precipitating factor in the production of hæmoglobinæmia. The almost constant finding of a positive Wassermann test in the blood of persons with paroxysmal hæmoglobinuria suggests that in some way syphilis may produce a hæmolysin in the blood.

Treatment.—Obviously, avoidance of cold is of primary importance in the prophylaxis of paroxysms. During the attacks plenty of fluids must be taken in order to avoid concentration of the urine. Unfortunately, antisyphilitic treatment is usually ineffective in preventing hæmoglobinuria.

HODGKIN'S DISEASE

(*Lymphadenoma*)

Ætiology.—Hodgkin's disease occurs more frequently in males than in females, and it is particularly prone to attack its victims during adolescence or early adult life. It occurs with equal frequency among rich and poor, and no country or climate seems exempt.

Symptoms.—The onset is usually gradual, and the first symptom noticed is an enlargement of some group of glands, most frequently in the neck. Later other groups of lymph glands become involved, the patient loses weight, becomes anæmic, and sometimes suffers from the effects of pressure

of the glands on neighbouring structures. The symptoms referable to various organs are described separately below.

1. *Lymphatic Glands.*—The typical glands of Hodgkin's disease are enlarged and discrete, with no tendency to adhere either to the skin or to the deeper structures ; on palpation they feel elastic, but in the later stages become harder. They are neither painful nor tender. Eventually most of the lymph glands in the body become affected, but at the onset the most common site for glandular enlargement is the posterior triangle of the neck on one or other side. As a result of X-ray treatment or secondary infection, adhesions to the skin very occasionally occur, but in any early case the finding of a gland which is definitely adherent contraindicates a diagnosis of Hodgkin's disease.

2. *Spleen.*—This is enlarged in about half the cases. It seldom extends more than 2 in. below the costal margin and is not tender.

3. *Cutaneous Manifestations.*—Pruritus is sometimes an early symptom. It may continue throughout and prove a formidable problem in treatment. More rarely there are small deposits of lymphadenomatous tissue in the skin.

4. *Lungs.*—Enlarged mediastinal glands may compress the lung. Pleural effusions occur in the later stages, due either to pressure on veins or to direct involvement of the pleura.

5. *Blood.*—There is nothing typical about the blood picture in Hodgkin's disease. Sooner or later a severe hypochromic anæmia develops. Eosinophilia (above 10 per cent.) is found occasionally.

6. *Pyrexia.*—Nearly all patients with Hodgkin's disease are febrile at some time during its course. The fever is often low and irregular, but sometimes periods of pyrexia lasting five to ten days occur, with apyrexial intervals between the attacks. Pyrexia of this type often occurring without obvious enlargement of external glands is known as the *Pel-Ebstein Syndrome.* In such cases there is an enlargement of the mediastinal glands.

7. *Nervous System.*—Pressure of enlarged glands upon nerves often gives rise to pain. In rare cases a paraplegia develops as the result of pressure on the cord.

Pathology.—The cause of Hodgkin's disease remains undiscovered. Gordon has been able to produce an encephalitis in rabbits by intracerebral injection of lymphadenomatous glands, and it has been suggested that the disease is due to an unknown virus. It certainly is not due to tuberculous infection, although the latter may sometimes be present as a complication. Nor is there any evidence that it is in the nature of a malignant growth except its invariably fatal issue.

At autopsy the lymphatic glands are found to be enlarged, white, and homogeneous. The amount of fibrous tissue varies with the chronicity of the condition. Suppuration or caseation is rare, except in cases complicated by tuberculosis. Microscopically there is an overgrowth of endothelial cells and fibrous tissue. The most characteristic histological features are the presence of giant cells, often with two or more nuclei and numerous eosinophil leucocytes. The spleen is moderately enlarged, and on section shows greyish-white areas about the size of peas which, under the microscope, show similar changes to those found in the lymph glands. These small deposits are scattered throughout the spleen, which is usually described as " hard-bake." Similar deposits occur in other organs, particularly in the liver and intestinal tract.

Differential Diagnosis.—Although typical cases of Hodgkin's disease can be diagnosed on clinical grounds, it is often impossible to be certain of the diagnosis without excising a gland. Sometimes even histological examination of a gland may leave the diagnosis in doubt. The resemblance between the glandular enlargement of Hodgkin's disease and that due to tuberculosis is so close that mistakes are very common, unless a gland be removed for section. Examination of a blood film will readily exclude lymphatic leukæmia, while the enlarged glands in syphilis are usually smaller, harder, and more shotty to the touch than in Hodgkin's disease, and the epitrochlear glands are seldom enlarged in the latter disease. Glandular enlargements in the neck due to septic teeth or infections of the scalp may be mistaken for Hodgkin's disease. Malignant glands in the neck are usually localised and extremely hard. In lymphosarcoma the glands tend to produce pressure symptoms earlier than in Hodgkin's disease, but in cases of doubt, biopsy is necessary. Lastly, glandular fever may produce a generalised glandular enlargement, but in this disease there is tenderness on palpation of the glands, a relative mononucleosis in the blood and the heterophile antibody reaction will be positive.

In some cases of Hodgkin's disease where the superficial lymphatic glands do not become enlarged until late in the disease, the severe anæmia which sometimes develops may suggest pernicious or other form of anæmia. A pyrexia without obvious cause, particularly if it assumes the typical Pel-Ebstein type, should always arouse a suspicion of Hodgkin's disease in the mediastinal or retroperitoneal glands. An X-ray of the chest may demonstrate the presence of masses in the mediastinum.

Treatment.—Unfortunately there is no specific treatment for Hodgkin's disease. Although temporary improvements may occur from time to time, the disease pursues a relentless downhill course, until death occurs as the result of anæmia and exhaustion or from the pressure effects of the enlarged glands on vital organs. In the early stages deep X-ray therapy and radium usually produce a rapid diminution in the size of the glands, but unfortunately relapse always occurs and further radiation treatment is usually ineffective. The only drug that appears to have any beneficial action is arsenic taken in large doses. With severe pruritus, veronal in 10 gr. doses may be effective.

J. J. Conybeare.
F. A. Knott.

SARCOIDOSIS

Several syndromes of which Boeck described the first in 1889 are now regarded as variants of one disease entitled Sarcoidosis, and in the aggregate these disorders though uncommon are not rare. A characteristic chronic granulomatous inflammation with involvement of the reticulo-endothelial system occurs. Any organ of the body may be affected, and although investigation often shows that the disease is generalised certain clinical patterns of involvement predominate. These include the following :—

Eyes.—Uveoparotitis (Heerfordt), Iridocyclitis, Mikulicz's disease.

Skin.—Sarcoid (Boeck, and Darier-Roussy), Lupus pernio. Angiolupoid.

Bones.—Osteitis multiplex cystoides (Jungling).

Lymph Nodes.—Benign Lymphogranulomatosis (Schaumann).

Lungs.—Disseminated nodular and reticular pulmonary lesions with local glandular involvement. Non-caseating tuberculosis (Pinner), Pseudo-tuberculosis (Snapper).

Other Organs.—(Spleen, liver, bone marrow, heart, nervous system, etc.) Universal large-celled sclerosing hyperplasia (Schurmann). Chronic epithelioid cell reticuloendotheliosis (Leitner).

Ætiology.—As is the case with Hodgkin's disease, sarcoidosis is often regarded as a reticulosis of unknown cause.

Among other possible ætiological factors tuberculosis seems the most probable, but the evidence is inconclusive. Tubercle bacilli have only occasionally been demonstrated in sarcoid lesions ; and although tubercles are formed their histology is not typically tuberculous, indeed similar structures have been described in leprosy, Leishmaniasis, undulant fever, syphilis, typhus, and rheumatism. On the other hand, the geographical distribution of tuberculosis and sarcoidosis is similar—in African negroes, for example, sarcoidosis is almost unknown, in North American negroes it is fairly common—and tuberculosis in certain animals such as the horse and rat has a sarcoid histology. The Mantoux reaction in sarcoidosis is usually negative whatever the patient's age, and if B.C.G. (*vide* p. 98) is injected subcutaneously the adducent lymph glands develop a sarcoid reaction, whereas in a normal individual previously uninfected with tuberculosis the same injection provokes a typical tuberculous lymphadenitis. That constitution may play a part is further suggested, since the disease has been observed in members of the same family.

The greatest prevalence of the disease occurs between the ages of twenty and forty, though instances in infancy and old age have been recorded. The sexes are equally affected. A considerable proportion of cases die of undoubted acute miliary tuberculosis.

Pathology.—The lymph glands, skin, eyes, lungs, spleen, and bones are most often involved. Whatever the site, the lesion is characteristically a chronic granulomatous inflammation, though the particular tissue involved greatly modifies the macroscopic appearances.

Histological examination shows that tubercles are formed within a periphery of hyaline connective tissue. These tubercles sometimes contain one or more giant cells, but unlike those due to tuberculosis they usually consist almost entirely of rather large round epithelioid cells surrounded by a single layer of lymphocytes. Caseation, too, is absent or very slight, as is calcification. The adjacent fibrous tissue reaction may be well marked, and, of course, many such tubercles may coalesce.

Clinical Features.—Very considerable variation exists in the pattern of symptoms and signs presented. Furthermore, though most cases follow a chronic course, in some this may be interrupted by relatively acute exacerbations, while in a few the disease is comparatively acute from onset to termination. In such cases, and when recrudescence of activity occurs in more chronic examples, the lesions are as a rule generalised. They give rise to toxæmia with malaise, pyrexia usually less than 102° F., sweating, anorexia, loss of weight, and amenorrhœa, together commonly with widespread discrete lymphadenitis, splenomegaly, hypochromic anæmia, and diffuse pulmonary lesions. The last may cause some dyspnœa, slight cyanosis, and an unproductive cough. The blood sedimentation rate is raised. In

addition the particular focal characteristics of the syndrome into which the case falls will be evident. In uveoparotitis, for example, these may include iridocyclitis, which usually progresses and causes glaucoma and blindness, painless and probably symmetrical enlargement of the parotids, and transient seventh-nerve palsy; while in Boeck's sarcoid indolent hard red-brown nodules and plaques, for the most part on the face, are typical.

Quite often, however, generalisation does not occur, or cannot be demonstrated, and then symptoms and signs of constitutional disturbance are absent, and the local consequences are frequently those of a torpid protracted inflammation. Pain is not a feature of the disease except when ocular lesions are present, and then it is rarely severe.

Radiological Appearances.—Pulmonary involvement is often only revealed by radiological examination. The appearances which are due to involvement of the pulmonary lymphatic system, though commonly symmetrical, are not necessarily so when the lesions are developing. They consist of a diffuse reticulation upon which is superimposed a rather coarse widespread nodulation. A gross symmetrical hilar and mediastinal lymphadenopathy is usually associated. Osteitis multiplex cystoides affects the short bones of the hands and feet, and to X-ray the lesions appear as clear cystic spaces slightly expanding the bone, and situated usually toward its distal end.

Diagnosis.—Certain syndromes, for example, Mikulicz's disease, are unique, and so offer little difficulty in diagnosis. In others and when generalisation has occurred, frequently the bizarre and typical distribution of lesions will be highly suggestive, particularly if the short bones are involved. The chronicity of the process, and its low-grade toxæmia with resulting constitutional upset, the anergy to tuberculin as shown by the Mantoux reaction, radiological appearances of the chest, and finally the histological appearances of a biopsy specimen will frequently suffice to identify the disease.

Hodgkin's disease, possibly lymphosarcoma, carcinomatosis, and widespread glandular tuberculosis may exceptionally cause difficulty in diagnosis, but will usually be distinguished by the last two investigations. It may, despite investigation, be quite impossible to distinguish chronic miliary tuberculosis from sarcoidosis, indeed it is not certain that a fundamental difference exists. The discovery, however, of living tubercle bacilli, the histological appearances and especially the demonstration of caseation or calcification in any of the lesions, a greater preponderance of pulmonary nodulation, and less marked hilar lymphadenopathy to X-ray, though not decisive are all rather more suggestive of the former disorder.

Prognosis.—Most authors maintain that the prognosis in sarcoidosis is good. However, from the instances occurring in which death results from involvement of the heart and brain, and the even more numerous cases in which tuberculosis is a fatal complication, it would seem probable that the benignity of the disease has been overemphasised. Local lesions have a variable prognosis. Thus, usually the skin lesions slowly disappear, and they never ulcerate. On the other hand, loss of vision is very common when the eyes are involved.

Treatment.—No really effective therapy is known. In the author's opinion the most important single measure is long continued rest in bed followed by a protracted convalescence on sanatorium lines, when the disease is generalised, or, if the eyes are involved.

X-ray therapy has proved to be of value in some cases of Mikulicz's disease, and has also been employed with benefit by the author when the mediastinal lymph glands are involved. Its use might be extended in other instances.

Tuberculin and ultra-violet light have been advocated. Their value is doubtful, but there is no doubt of their dangerous qualities when either the lungs or the eyes are affected. Local palliative procedures are available when necessary, depending on the site of the lesions.

W. D. W. Brooks.

LYMPHOSARCOMA

Sarcomatous growths may originate in lymphoid tissue in any part of the body, but most commonly in the lymphatic glands. The symptoms depend mainly on the site of the glandular enlargement and on pressure effects on surrounding parts. With involvement of the mediastinal glands obstruction of the superior vena cava is likely to occur, and results in venous congestion of the upper part of the body.

Glands affected by lymphosarcoma are at first painless, and may remain unattached to the skin and surrounding structures. Eventually, however, these will become involved. Often several groups of glands may be enlarged simultaneously, and the clinical condition closely resembles Hodgkin's disease. In order to arrive at a definite diagnosis, a biopsy is often necessary.

If the lymphosarcomatous glands are localised they should be excised, but when disseminated or very adherent they can often be rapidly reduced in size by deep X-ray therapy. Even after apparently complete removal a course of X-ray treatment is advisable. The ultimate outlook is always bad, particularly in cases with involvement of mediastinal glands.

SPLENIC ENLARGEMENT

Complete removal of the spleen is not incompatible with perfect health, and its physiological functions can undoubtedly be taken on by other organs. In adult life the spleen, as part of the reticulo-endothelial system, plays an important part in the destruction of red blood corpuscles and in the metabolism of iron. It also acts as a storehouse for a surplus supply of red corpuscles, which can be readily mobilised into the general circulation when required, as, for instance, after severe hæmorrhage. It may also be concerned in the formation of antibodies as a reaction to infection.

Splenic Enlargement.—This may occur in a variety of morbid conditions : (i) in acute infective conditions, *e.g.*, typhoid fever, septicæmia, subacute bacterial endocarditis ; (ii) in chronic infections, *e.g.*, tuberculosis, congenital syphilis, possibly Hodgkin's disease, glandular fever ; (iii) in protozoal infections, *e.g.*, malaria, kala-azar ; (iv) in diseases of the blood and blood-forming organs, *e.g.*, pernicious anæmia, the leukæmias, acholuric jaundice, polycythæmia, and splenic anæmia ; (v) conditions where there is interference with the circulatory system of the spleen, *e.g.*, thrombosis of the splenic vein, cirrhosis of the liver, or splenic infarction; (vi) in conditions in which the spleen appears to store abnormal metabolites, *e.g.*, amyloid disease ;

(vii) in very rare instances of neoplastic secondary deposits, *e.g.*, melanotic sarcoma.

In most of the diseases classified above, splenic enlargement is but one, and often not the most prominent feature; but in the group of splenic enlargements known as splenic anæmia it is possible that the spleen is the primary seat of disease.

To palpate for an enlarged spleen the examiner should stand on the right-hand side of the recumbent patient and place his right hand flat upon the abdomen with the fingers near the left costal margin. With the left hand the left lower ribs are pressed firmly forwards, and the patient is instructed to take a deep, slow breath. If the spleen is enlarged, it will be felt to descend from under the costal margin against the examining fingers. The *characteristic features of a splenic tumour* are: (i) a sharp lower edge in which sometimes a notch is palpable; (ii) the tumour is superficial, dull on percussion, and the hand cannot get above the tumour; (iii) unless very large, it does not extend into the loin. The direction of enlargement is downwards and inwards towards the umbilicus, and the tumour is found to move on respiration. With great enlargement there may be visible bulging in the left hypochondrium. In acute infections the spleen is often tender and rather soft, but unless it is possible to feel a sharp lower margin it is dangerous to diagnose splenic enlargement.

Splenic Anæmia

It is uncertain whether so-called splenic anæmia has any separate clinical entity. Probably many of the cases thus diagnosed were in reality instances of cirrhosis of various types with enlarged spleens, acholuric jaundice, chronic types of purpura, Gaucher's splenomegaly, or even leukæmia. Certainly as knowledge of blood diseases has increased, splenic anæmia has become a less frequent diagnosis.

The relationship between splenic anæmia and the condition of splenomegaly and cirrhosis of the liver, described in Italy by Banti and known by his name, has been a matter of dispute. It is often maintained that Banti's disease represents a late stage in splenic anæmia. There is, however, little evidence in support of this assumption, though cirrhosis of the liver is often accompanied by more or less splenic enlargement. Many cases of splenic anæmia run their course without evidence of cirrhosis, and cases corresponding to Banti's description of his disease are rare, if not unknown, in England.

Ætiology and Pathology.—As it is uncertain whether splenic anæmia is a clinical or pathological entity, nothing is known of its ætiology and pathology. There is no evidence of hæmolysis and no constant pathological findings. When hæmatemesis occurs it is presumably due to rupture of œsophageal varices as in cirrhosis.

Symptoms.—The onset of the disease is insidious, though occasionally hæmatemesis may be the first symptom to call attention to the condition. The spleen is much enlarged, hard, and often reaches the umbilicus or beyond. Anæmia of a microcytic type with a low colour index and a leucopenia is usually present, quite apart from severe hæmatemesis, though when this occurs it naturally aggravates the anæmia. Hæmatemesis is the most important and dangerous symptom, and may be both profuse and recurring.

After the disease has lasted for some years there is sometimes evidence of the onset of cirrhosis of the liver. At first this organ may be enlarged, but eventually it tends to diminish in size, while jaundice, ascites, and emaciation develop. The patient usually suffers from the symptoms common to all anæmias, such as breathlessness, pallor, palpitation, and lassitude. As in other anæmias, a hæmic murmur is often present over the base of the heart. Often the weight of the enlarged spleen produces dragging pains in the abdomen. Occasionally purpuric spots are seen on the skin.

Course and Prognosis.—The disease is a very chronic one, and occasionally may last twenty years or more. Spontaneous recovery may occur, but more often the condition slowly progresses until it terminates in death from intercurrent infections, hæmatemesis, or cirrhosis.

Differential Diagnosis.—The occurrence of splenomegaly in several members of a family suggests Gaucher's splenomegaly or acholuric jaundice. If splenomegaly is associated with purpura or recurrent hæmorrhage from the nose, gums, or elsewhere, purpura hæmorrhagica is a possibility. The leucocyte count will be characteristic in leukæmia.

Treatment.—Splenectomy is often advised in cases diagnosed as splenic anæmia. The results of the operation are often disappointing and do not compare with those of splenectomy in acholuric jaundice or thrombocytopenic purpura. Moreover, the mortality is considerable. Large doses of iron are often beneficial and transfusion may be required, especially if the patient has had severe hæmatemesis.

Gaucher's Splenomegaly.—This disease was formerly considered to be identical with splenic anæmia. It differs from the latter in being frequently familial, though not hereditary. The spleen is enormously enlarged, but the anæmia is seldom as severe as in splenic anæmia. Hæmatemesis very rarely occurs, but slight epistaxis and bleeding from the gums is common. The liver is very large throughout the disease, but cirrhosis does not occur. In spite of the great enlargement of spleen and liver the disease is compatible with relatively good health for many years. The spleen, liver, lymph glands, and bone marrow are packed with characteristic large "foamy" lipoid cells of an endothelial type. Splenectomy is not advisable.

J. J. Conybeare.
F. A. Knott.

DISEASES OF THE ALIMENTARY CANAL

GENERAL CONSIDERATIONS

BOTH in hospital and private practice very large numbers of patients are encountered whose main symptoms are rightly or wrongly referred to the abdomen. In consequence, one of the most frequent and yet most difficult problems which face the medical attendant is to decide to what extent the internal organs of digestion are affected by disease. It is important to realise that of the many patients who complain of "indigestion," only a relatively small proportion suffer from organic lesions such as a peptic ulcer. Often the symptoms referred by the patient to his abdominal viscera are in reality but reflex expressions of diseases elsewhere or an indication of a failure on the part of the patient to adjust himself satisfactorily to his environment.

Although "nervous indigestion" is extremely common, it is most important, both from the point of view of the patient and of the doctor, that such patients should not be labelled as neurotics until a thorough examination and investigation has so far as possible excluded the presence of an organic lesion. We must all of us be familiar with those unfortunate individuals in whom a failure on the part of the doctor to diagnose organic disease in its earlier stages has allowed it to progress to a condition in which cure is difficult or impossible.

In cases of suspected abdominal disease a careful history is of the utmost importance. The patient should be allowed to tell his own story. Particular attention should be devoted to the duration of his symptoms, the occurrence of remissions, the nature of his pain and its relationship to meals, the presence of constipation or diarrhœa. Apart from the actual information obtained in taking a careful history, the contact which it establishes between doctor and patient is of great value in enabling the physician to gain an insight into the mental attitude of the patient and his degree of sensibility to pain, points which are of great value in diagnosis.

A thorough physical examination of *all the systems* of the body must never be omitted. Not infrequently this may reveal some unsuspected lesion, to which the abdominal symptoms are purely secondary. Thus, for example, the earliest symptoms of phthisis may be dyspepsia, or attacks of abdominal pain or vomiting may be due to tabes dorsalis, lead-poisoning, or uræmia.

Before attempting to examine the abdomen, attention must be paid to the following points: (i) the patient should lie comfortably on his back with his head slightly raised and supported on a pillow; (ii) the abdomen must be well and evenly illuminated; (iii) the hands of the examiner must be thoroughly warm. Neglect of any of these precautions will render efficient examination difficult or impossible.

It is well to carry out an abdominal examination in a routine manner, beginning with *inspection* of the whole abdomen and lower part of the

chest. The patient should be asked to indicate exactly the point at which any pain is felt. Note should be made of the general appearance of the abdomen, whether distended or flattened, and in the former case whether the distension is local or general. It is also easy to see whether there is any restriction of the normal abdominal respiratory movements. Lastly, it is important to look for visible peristalsis; this may often be elicited by flicking the abdominal wall with a finger. In very thin subjects it is sometimes possible to see the peristaltic movements of a normal small intestine, but as a rule visible peristalsis is of great significance, and indicates obstruction at some point in the alimentary canal. In such cases the peristaltic waves are repeated at intervals in the same area and direction.

Following inspection, the abdomen is examined by *palpation*. It is important to gain the patient's confidence by beginning with gentle palpation with the hand flat on the abdomen. If one side or area of the abdomen is the seat of pain, the examination should be commenced by palpating some other part. During palpation cultivate a flow of small talk to the patient with a view to distracting his attention from what is being done, and never ask whether pressure at any particular point is painful. If a careful watch is kept on the patient's face, the tender points, if any, will be instantly revealed by his expression, without the possibility of suggestion on the part of the examiner. The extent and localisation of rigidity of the muscular wall should be noted, and an attempt made by diverting the patient's attention to abolish it. If the rigidity is persistent, and especially if it is associated with local tenderness on pressure, it will usually indicate involvement of the peritoneum. During palpation, tumours may be detected, and an attempt should then be made to determine their mobility, more particularly with reference to respiratory movements. In addition to the central part of the abdomen, the flanks must be palpated bimanually; while doing so the examiner should be on the same side of the patient as the flank to be examined, and should place one hand behind, immediately below the ribs, while the other presses on the front of the abdomen; the patient is instructed to take deep breaths, and during inspiration tumours in the loin, such as an enlarged or unduly mobile kidney, may be felt to descend and may be gripped between the fingers. If the patient is cold, palpation is rendered very difficult.

Percussion of the abdomen is, as a rule, of little value except for the detection of "shifting dullness" when there is free fluid in the peritoneal cavity. Auscultation of the abdomen is of value in the diagnosis of acute abdominal conditions as the peristaltic movements of the intestines may be audible, thus rendering a diagnosis of peritonitis unlikely. Rarely a friction rub may be heard over an inflamed organ, such as the spleen or liver.

Much stress used to be laid on the detection of areas of cutaneous hyperæsthesia, but these are usually if not always the result of suggestion on the part of the examiner. If the stomach is much dilated, a succussion splash may be heard when sudden pressure is exerted upon the epigastrium. This indicates delay in emptying, unless a meal has been taken within two hours of examination.

The importance of investigations such as X-ray examinations, test meals, and chemical examinations of the fæces cannot be overestimated. During the last fifteen years, advances in radiological technique have greatly increased the value of opaque meals and enemata. Valuable though these

aids to diagnosis may be, it is still true that they are an addition to, and not a substitute for, a carefully taken history and a thorough physical examination. Every patient with digestive symptoms, which fail to clear up within a reasonably short period, should be advised to undergo a thorough investigation to exclude serious organic disease. Such an investigation not infrequently may reveal the presence of an organic lesion which has been entirely unsuspected from a consideration of the history and the physical examination. Negative findings are also of great value in reassuring not only the patient but the medical attendant.

Rectal examination should be made in every case with abdominal symptoms. If this is neglected, there is always the risk of overlooking the presence of a rectal growth or of secondary deposits in the pelvis. Sigmoidoscopy is also frequently necessary (*vide* p. 328).

DISEASES OF THE MOUTH

Oral Sepsis

Pyorrhœa Alveolaris.—In this condition pockets are formed between the teeth and the gum margin, in which food debris and pus collect. The alveolar margin becomes gradually absorbed as a result of a rarefying osteitis and the pockets increase in depth, so that eventually the teeth become loose. The gums become inflamed and bleed readily when touched, and by pressure on the gum margins pus can be squeezed out. During mastication considerable amounts of pus are swallowed and may produce chronic gastritis, or possibly peptic ulceration. Pyorrhœa often causes increased salivation, an unpleasant taste in the mouth, and foul breath.

Pyorrhœa may be prevented by careful attention to the cleanliness of the teeth, and food debris must not be allowed to collect around them. Regular visits should be paid to a dental surgeon at least every six months.

Apical Infection.—This is a more insidious condition than pyorrhœa, and is more likely to be overlooked. The affected teeth are always dead, but may appear healthy. X-ray, however, shows pathological changes at the root. The condition is specially liable to occur around septic stumps and in teeth which have been devitalised by the dental surgeon. From its situation it is obvious that free drainage cannot take place, and there is great liability to the absorption of toxins or even of micro-organisms, which may give rise to an infective arthritis, fibrositis, or neuritis, and even to septicæmia and infective endocarditis. The organism most frequently found on culture is the *Streptococcus viridans*. Following extraction of infected teeth there is often a transient bacteriæmia. The only satisfactory way of establishing the absence of apical infection or of osteitis of the alveolar margin is to take X-ray films of the teeth. An apical abscess, or indeed even a dead tooth, is always a potential source of danger, which can only be removed by extraction of the tooth and treatment of the cavity in the jaw.

Before the extraction of infected teeth the patient should suck penicillin pastilles, or if many teeth are to be extracted he should be given penicillin intramuscularly. In any case the teeth should be scaled and cleaned before extraction.

Stomatitis

Catarrhal Stomatitis occurs in infants with febrile illnesses. In adults it may result from excessive smoking, dental sepsis, or overdosage with mercury or other heavy metals. A glycerin and borax mouthwash is effective.

Aphthous Stomatitis.—Slightly raised vesicles form on the mucous membrane of the lips and cheeks, which quickly rupture and produce small greyish ulcers with a red areola around them. The ulcers heal spontaneously, but often recur. Treatment is as a rule ineffective, but sometimes local application of silver nitrate gives relief.

Thrush.—The condition popularly known as thrush is a parasitic stomatitis due to a fungus, *Oidium albicans*. It infects chiefly the mouths of ill-nourished infants, especially if bottle-fed, but may also occur in debilitated adults. The mouth is dry, and scattered over the tongue, gums, cheeks, and palate there are white patches slightly raised above the surrounding mucous membrane.

The mouth should be kept clean with cotton wool soaked in the following mixture : potassium chlorate, 10 gr. ; glycerinum boracis, ad 1 oz., and the patches painted with 1 per cent. gentian violet solution. With this treatment and attention to the general health, recovery is usually rapid.

Ulcerative Stomatitis (*vide* Vincent's angina, p. 445).

Gangrenous Stomatitis (Cancrum Oris).—In debilitated children ulceration occurs on the cheek or gum and the surrounding tissues become black and gangrenous. Although the temperature is seldom high, death occurs rapidly from exhaustion or pulmonary infection. The gangrenous area should be excised early.

Ludwig's Angina is an acute infection of the floor of the mouth, producing marked swelling under the jaw and in the neck. The condition develops rapidly, with severe constitutional symptoms. Treatment is surgical.

Disorders of the Salivary Glands

Ptyalism, or excessive secretion of saliva, most commonly is due to oral sepsis. It may also occur reflexly in trigeminal neuralgia or from irritation in the œsophagus or hyperchlorhydria. It also occurs in post-encephalitic Parkinsonism. Iodides and mercury are partially excreted in the saliva, and may lead to ptyalism. It is also common in neurotic subjects without obvious organic disease.

Treatment of ptyalism depends on the underlying condition, but belladonna or atropine may produce a symptomatic improvement. In ptyalism associated with anxiety neuroses bromides or phenobarbitone are of value.

Xerostomia (deficient secretion of saliva) is usually present in the acute fevers, and leads to a dry and septic condition of the mouth and tongue. It may occur also in diabetes and severe diarrhœa, owing to the large amount of fluid lost in the urine and fæces. Atropine and belladonna also diminish the secretion of saliva.

Specific Parotitis, or Mumps (*vide* p. 32).

Septic Parotitis.—This is a dangerous complication of any prolonged febrile illness, such as typhoid fever. For prophylaxis careful attention to

the mouth is essential. If suppuration occurs, the glands need incision and drainage.

Mikulicz's Disease.—Enlargement of the salivary and lachrymal glands occurs as a feature in sarcoidosis (*vide* p. 285).

DISEASES OF THE ŒSOPHAGUS

Anatomy and Physiology.—The œsophagus extends from the termination of the pharynx at the lower border of the cricoid cartilage to the cardiac orifice of the stomach. Its average length in an adult is 10 in., but more important from the clinical point of view is the distance from the front teeth to the cardiac orifice, which is usually about 18 in. The relations of the œsophagus are important, as surrounding structures may be involved in disease of the organ, or, conversely, pathological conditions in the neighbourhood of the œsophagus may produce obstruction of its lumen.

From its commencement in the neck the œsophagus lies immediately behind and in close contact with the trachea, while the recurrent laryngeal nerves lie in the grooves between the two on either side. In the thorax the œsophagus passes through the superior and posterior mediastina, crossed by the left bronchus at the level of the fifth dorsal vertebra. On passing an œsophagoscope two well-defined constrictions are encountered, one the crico-pharyngeal sphincter at the level of the sixth cervical vertebra, the other the passage through the diaphragm at the level of the tenth dorsal vertebra. Carcinomata and strictures caused by corrosives are frequently seen at the level of the fifth dorsal vertebra, where the left bronchus crosses the œsophagus. There is evidently a functional delay at this level. The arch of the aorta lies in relation to the left side of the œsophagus.

Unlike other parts of the alimentary canal, the mucous membrane of the œsophagus is sensitive to thermal stimuli ; if hot or cold fluids be drunk or passed into the œsophagus through a rubber tube, a sensation of heat or cold is felt deep in the chest or epigastrium. At the point where the œsophagus enters the stomach is the cardiac sphincter, which is normally closed. Relaxation of the sphincter follows the swallowing reflex.

Œsophagitis and Œsophageal Ulcer

Acute œsophagitis may follow swallowing of hot or corrosive fluids or the impaction of a foreign body. Chronic œsophagitis, often with superficial erosions of the mucous membrane, occurs in achalasia of the cardia (*vide* p. 297). It may also be due to oral sepsis and alcoholism.

Peptic ulcer of the lower end of the œsophagus occurs as a complication of a congenital short œsophagus and thoracic stomach (*vide* p. 314).

Œsophageal Obstruction

Practically all the pathological conditions of the œsophagus show as their most prominent symptom difficulty in swallowing, known as dysphagia. The causes of œsophageal obstruction may be classified as follows :—

1. Malignant stricture of the œsophagus.

2. Non-malignant stricture.
   (*a*) Impaction of a foreign body in the œsophagus.
   (*b*) Cicatricial stenosis following trauma.
   (*c*) Gumma (excessively rare).
   (*d*) Peptic ulcer of the œsophagus.
   (*e*) Congenital stricture.
   (*f*) Chronic hypopharyngitis associated with Plummer-Vinson syndrome (*vide* p. 272).
3. Derangement of the neuromuscular mechanism.
   Achalasia of the cardia.
4. Pressure upon the œsophagus from without.
   (*a*) Goitre.
   (*b*) Aortic aneurysm and mediastinal tumours.
   (*c*) Pharyngeal diverticulum.
   (*d*) Diaphragmatic hernia.
5. Hysterical dysphagia.

In addition to the above, dysphagia may result from pathological conditions in the mouth and pharynx, such as growths of the tongue, tonsillitis, or retropharyngeal abscess. Palatal and pharyngeal paralysis may produce dysphagia, as, for example, in diphtheria, bulbar palsy, or myasthenia gravis.

Carcinoma of the Œsophagus

This is the most frequent cause of œsophageal obstruction over middle age. The onset is insidious ; at first there is nothing beyond an occasional tendency for solid food "to stick in the throat." This symptom, after intermissions lasting many weeks, becomes more frequent, until it is found impossible to swallow solids. Later there is difficulty even with fluids, and ultimately nothing can be taken at all. Attempts to swallow result in regurgitation, but as a rule pain is strikingly absent, though occasionally pain in the chest may be an early symptom. Death usually occurs from bronchopneumonia. Occasionally pressure on surrounding structures such as the recurrent laryngeal nerve produces a paralysis of the larynx with aphonia, which may occur before any dysphagia is noted.

Carcinoma of the œsophagus most commonly occurs in three situations : at the junction of the pharynx and œsophagus, at the point where the œsophagus is slightly narrowed by the crossing of the left bronchus, and at the cardiac orifice. Often the patient is able from his subjective sensations to localise fairly accurately the site of the obstruction.

Although it is usually easy to diagnose a growth of the œsophagus on clinical grounds in view of the age of the patient, the history of the gradual onset of the dysphagia, and the rapid emaciation, the diagnosis must be confirmed by further investigations. A barium swallow, using a thick barium emulsion, will show irregularity in the lumen of the œsophagus and partial or complete obstruction is readily demonstrated. Incidentally, an X-ray examination may reveal pathological conditions of other organs, such as an aortic aneurysm. The growth can be viewed through an œsophagoscope, and a piece removed for histological section if required. On no account should a bougie be passed. Quite apart from the possible

PLATE 12

Carcinoma of the lower end of the œsophagus. The long and irregular stricture is shown with moderate dilatation of the œsophagus above.
(From film by Dr T. H. Hills.)

[*To face page* 296.

PLATE 13

Achalasia of the cardia, showing the greatly dilated and elongated œsophagus. (From film by Dr T. H. Hills.)

[*To face page* 297.

though improbable perforation of an aortic aneurysm, there is a very grave risk of perforating the œsophageal wall immediately above the growth.

Occasionally a carcinoma of the stomach near the cardiac orifice may produce dysphagia as an early symptom. Such cases may be misdiagnosed as œsophageal growths, but X-ray examination and œsophagoscopy will settle the diagnosis. Early growths near the cardia have occasionally been removed successfully.

With early diagnosis surgical excision is occasionally possible, but in most cases treatment is palliative, and death usually results within two years or less. If the obstruction is complete a gastrostomy may be required, but life subsequently is a misery. With incomplete obstruction various palliative measures are available, which in most cases enable the patient to swallow moderately satisfactorily. These include deep X-ray therapy, implantation of radon seeds, diathermy of the growth, and intubation with Souttar's tube.

Non-malignant Stricture of the Œsophagus.—This condition most commonly follows the swallowing of corrosive fluids, either accidentally or with suicidal intent. The cicatricial stricture which develops is treated by dilatation which must be repeated at intervals.

Achalasia of the Cardia

This type of dysphagia was in the past known as cardiospasm, on the assumption that it was due to spasm of the cardiac sphincter. The term "achalasia" was introduced by Hurst to indicate that the obstruction, which undoubtedly exists, is due to a failure to relax rather than to increased tone. The condition is not uncommon, and in young patients is the most frequent cause of obstruction at the lower end of the œsophagus.

Pathology.—No organic obstruction is found at the cardiac sphincter, and the muscle fibres in this region show no signs of any hypertrophy. Normally, a peristaltic wave passing down the œsophagus is accompanied by relaxation of the sphincter. It has been suggested that in achalasia this does not occur, and the swallowed food is retained in the œsophagus. This is enormously dilated and hypertrophied in every case whatever the duration of the symptoms. This suggests that dilatation of the œsophagus is an essential part of the pathology of this condition. The failure of the cardia to relax is probably due to some derangement, functional or organic, in the neuro-muscular tissue known as Auerbach's plexus. In long-standing cases the irritation produced by stagnating food produces œsophagitis.

Symptoms.—The condition is often sudden in onset, with occasional remissions lasting for weeks, months, or years. The patient feels the food stick at a point which he locates at the lower end of the sternum, and, though he does not complain of pain, there is a feeling of discomfort and fullness in the chest due to the filled œsophagus. Food is usually regurgitated soon after a meal, but there is no nausea or retching, and the vomited material consists of whatever has been eaten, without admixture of bile or hydrochloric acid. When a considerable amount of food or drink is taken, the weight of the column of fluid in the œsophagus, when the patient is standing erect, is usually sufficient to force some of the food through the sphincter. Undernutrition results in loss of weight, though, in contrast to cases of carcinoma, the general condition of the patient remains fairly good. The symptoms may last for many years with remissions, though

the radiological appearances remain constant regardless of changes in the symptomatology.

Diagnosis.—Although the symptoms and history may strongly suggest achalasia, the diagnosis should be confirmed radiologically. X-ray shows a greatly dilated œsophagus with vigorous peristaltic waves; the lower end of the œsophagus has a perfectly regular outline, which is quite different in appearance from the irregularity which is usually seen even in an early carcinoma (*vide* Plates 12 and 13).

Treatment.—Dilatation of the sphincter can be effected by passing Hurst's mercury bougies, rubber tubes of varying diameter closed at both ends and containing mercury in the lumen. The tube is both heavy and flexible and readily passes through the cardia, which it stretches. The patient should be taught to swallow the tube himself and for a time should use it before each meal. There is often a striking symptomatic improvement and the use of the tube can be discontinued. When there is much œsophagitis, lavage with normal saline is advisable. In intractable cases the cardiac orifice may be dilated manually when the stomach has been opened at a laparotomy.

Inhalation of amyl nitrite or nitroglycerine ($\frac{1}{100}$ gr.) dissolved under the tongue produce a transitory relaxation of the cardia.

Pressure on the Œsophagus from Without

Dysphagia due to aortic aneurysm, mediastinal tumour, and goitre is extremely rare, and other symptoms usually point to the correct diagnosis.

Diverticula of the Œsophagus.—What is sometimes described as a pulsion diverticulum of the œsophagus is really a pharyngeal pouch, which emerges in the posterior median line of the hypopharynx between the oblique and transverse portions of the inferior constrictor muscles. As the pouch enlarges it extends down into the posterior mediastinum, and by pressure on the œsophagus produces dysphagia. Food is often regurgitated when the pouch fills. The diagnosis is readily made with an opaque meal and X-rays, or by examination with the œsophagoscope. Where the symptoms are severe, pulsion diverticula may be removed surgically.

Traction diverticula are small and seldom cause symptoms. They are thought to be caused by adhesions of the œsophagus to surrounding structures, such as a tuberculous gland.

Hysterical Dysphagia

An alleged inability to swallow is sometimes encountered in hysterical patients. Occasionally it is associated with an idea that a foreign body is lodged in the throat. The patient usually complains of a lump in the neck, the so-called *globus hystericus*. In this type of case solids are sometimes more easily swallowed than fluids, a condition which is not likely to be present in a dysphagia due to any organic lesion. The passage of the heavy mercury tube may be useful in demonstrating to the patient that there is no blockage of the gullet, though, in addition, treatment of the general condition by psychotherapy is, of course, necessary.

DISEASES OF THE STOMACH AND DUODENUM

Although the diagnosis of gastric and duodenal lesions can often be made with fair certainty on the strength of a careful history of the symptoms

and a physical examination, various clinical investigations are available which are of the greatest value in helping to confirm a clinical diagnosis. These are (i) X-ray examination ; (ii) fractional test meal ; (iii) examination of fæces for occult blood ; (iv) gastroscopy.

X-ray Examination.—A barium meal done by a *really competent* radiologist is of the greatest value. It gives information regarding (i) the motility of the stomach and its rate of emptying ; (ii) the presence of organic lesions such as chronic peptic ulcer, hour-glass constriction, or carcinoma. The first part of the duodenum is visualised as a triangular shadow just above and to the right of the pyloric end of the stomach and is known as the " duodenal cap " from its shape. An X-ray diagnosis of duodenal ulcer may be made on persistent irregularity in the outline of the " cap," which is often tender on palpation.

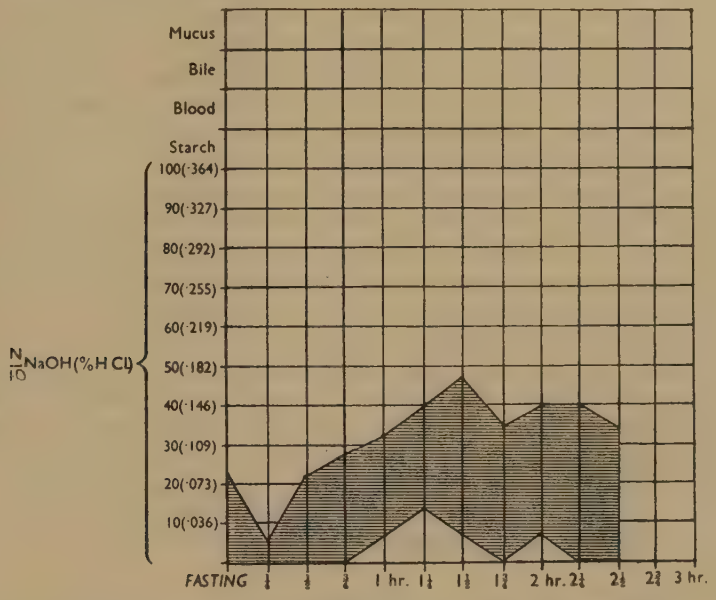

Fig. 10

Fractional test meal chart. The shaded area represents the limits of free HCl in 80 per cent. of normal persons.

In patients liable to constipation a mass of barium in the rectum may form a ball-valve obstruction which may necessitate manual removal under an anæsthetic. Therefore plenty of liquid paraffin should be given as early as possible after the radiological examination is completed.

Fractional Test Meals.—The patient, after fasting from the previous night, swallows a Ryle's tube. All the gastric contents are aspirated and measured ; the fluid obtained is known as the *resting juice.* A pint of fine oatmeal gruel is now swallowed with the tube still in position, and about 15 c.c. is aspirated at quarter-hourly intervals for about three hours or until no more can be obtained.

The specimens, including the resting juice, are examined macroscopically for the presence of blood and bile, and the percentage of free acid and the total acidity are estimated quantitatively, the results being plotted on a chart as shown in Fig. 10. The variations in the percentage of free acid in

normal persons are considerable and range from complete absence of free acid to extreme degrees of hyperchlorhydria. The specimens are also tested for the presence of starch and sugar, and the point at which these disappear is noted, as this indicates the time at which the meal has left the stomach. If the resting juice exceeds 50 c.c. or contains food debris, starch, or sugar in appreciable quantities, pyloric obstruction is probable. Pus or blood in the resting juice is suggestive of gastric carcinoma.

The acidity, both free and total, will depend on a number of factors, such as the rate and amount of gastric secretion, the rate of passage of the stomach contents into the duodenum, and the regurgitation of fluid from the duodenum into the stomach. The acidity tends to fall after about one and a half hours due to neutralisation by alkaline regurgitation from the duodenum, which is a feature of the normal digestive process.

A fractional test meal is of value in the diagnosis of carcinoma ; in this condition the free hydrochloric acid is usually absent or diminished, and blood may be present both in the resting juice and in the subsequent specimens. Obstruction of the pylorus by a cicatrising duodenal ulcer produces an acid curve which rises steadily and remains high after several hours. With duodenal ulcer the resting juice is often highly acid, and after a preliminary fall due to dilution on drinking the meal the subsequent specimens show a rapidly rising acidity with an increased rapidity of the passage of the meal out of the stomach. Normally the stomach should be empty, as judged by the absence of starch and sugar, within about two and a quarter hours. Ulcers of the body of the stomach do not as a rule exhibit any typical type of test-meal curve.

Even when no free acid is present in any of the specimens of gastric juice withdrawn, hypodermic injection of $\frac{1}{2}$ mg. of histamine may sometimes stimulate secretion of acid. When histamine fails to produce any acid the patient is said to have achylia gastrica rather than achlorhydria. Nearly all patients with pernicious anæmia show gastric achylia. After gastro-jejunostomy operations, achlorhydria is frequently present owing to the neutralisation of the gastric juice by alkaline secretion from the duodenum.

Occult Blood in the Fæces.—The patient must not take any meat, fish, or green vegetables for at least three days before the test. Provided bleeding from the gums is excluded, the finding of occult blood indicates bleeding from the alimentary tract. The examination should include a guaiac or benzidine test and spectroscopic examination for hæmatoporphyrin and acid hæmatin. The finding of hæmatoporphyrin shows that the bleeding is from the upper alimentary tract, and when acid hæmatin is present the amount of bleeding is considerable, as, for example, in gastric carcinoma.

Gastroscopy. — With a flexible gastroscope, the greater part of the stomach can be visualised and the discomfort to the patient is slight. The gastroscope is an aid to diagnosis in (i) shallow gastric ulcers and erosions, which the X-ray fails to visualise ; (ii) inflammatory or ulcerative conditions around a gastro-jejunal stoma ; (iii) chronic gastritis with or without erosions. Thus it may be of great value in revealing the cause of hæmatemesis in cases where the X-ray findings have been negative.

Gastroscopy is also of value in controlling the medical treatment of gastric ulcer. Even when the X-ray no longer shows a crater and occult blood has disappeared from the fæces, the gastroscope may show that the

ulcer is not yet completely healed and that several further weeks of strict treatment are required.

Unfortunately duodenal ulcers are not visible through the gastroscope, nor is the instrument always of value in deciding whether an ulcer is innocent or malignant. Negative gastroscopic findings may be, however, of great value in excluding organic disease of the stomach in doubtful cases. Needless to say, the gastroscope is only of value in the hands of one who has had considerable experience.

ORGANIC DISEASES OF THE STOMACH AND DUODENUM

Acute Gastritis

Acute Gastritis.—This affection is so common that there can be but few readers who have not had personal experience of it. The most frequent causes are excessive consumption of alcohol or the eating of food that has undergone decomposition as the result of bacterial action. As a rule abdominal discomfort rather than pain, nausea, a furred tongue, and vomiting are the most prominent features. Food poisoning is dealt with elsewhere (*vide* p. 200). During the acute stage the patient has marked anorexia. The vomit contains no free acid, but there is considerable excess of mucus. The gastric contents are often retained in the stomach for an abnormally long period. Attacks of acute gastritis may undoubtedly be provoked by chill, especially in the tropics. Most cases cure themselves, as abstinence from food for some hours is usually all that is required.

Acute gastritis also occurs in infections, such as scarlet fever and influenza, particularly at the onset of the disease.

Acute Phlegmonous Gastritis.—This follows the swallowing of corrosives such as strong acids or alkalis. There is intense pain, with vomiting and collapse. If recovery takes place, cicatricial stenosis of the pylorus may occur.

Chronic Gastritis

Whereas in the past chronic gastritis was only regarded as common among alcoholics, it is now becoming more widely recognised that the condition is not infrequent, especially in persons of over middle age. Apart from its symptoms, the presence of gastritis may be determined by the fractional test meal and the gastroscope. Hydrochloric acid is either low or absent and an excess of mucus is common.

The symptoms of chronic gastritis are usually characteristic. Morning anorexia, nausea, and vomiting are prominent features. The vomit consists only of swallowed mucus and saliva, and is small in amount. The appetite and digestion improve as the day wears on, and by the evening the patient usually feels fairly fit. Sometimes there may be a sensation of fullness and discomfort in the epigastrium, but this seldom amounts to real pain. The tongue is thickly furred.

The conditions which commonly predispose to the development of chronic gastritis are given below :—

1. Alcohol taken regularly in considerable amount.
2. Faulty habits as regards feeding, *e.g.*, hurried meals ; defective mastication ; excessive tea, coffee, or tobacco.

3. Septic conditions in the mouth or nasopharynx.
4. Congestion of the gastric mucous membrane in chronic heart disease.
5. Chronic infections, particularly phthisis.

How far chronic gastritis can be regarded as a precursor of more serious conditions, such as peptic ulcer and carcinoma, remains doubtful. It is certain, however, that acute erosions are often present which may cause severe hæmorrhage, and quite possibly develop into chronic peptic ulcer.

Treatment consists in persuading the patient to readjust his daily routine, where this appears to be at fault. Perhaps the easiest method of achieving this object is spa treatment, where regular habits and diet often work wonders, quite apart from the virtues of the waters. Septic teeth or gums must be dealt with. Even in cases in which alcohol is not the cause of the condition it should be absolutely forbidden, at any rate for many months. A gentian and soda mixture (soda bicarb., 15 gr. ; spirit. ammon. aromat., 30 minims ; inf. gent. co., ad $\frac{1}{2}$ oz.) is often useful in stimulating the appetite. Dilute hydrochloric acid B.P. may be given in doses up to 1 drachm, taken with half a pint of sweetened lemonade at meals. In intractable cases daily lavage of the stomach before breakfast with hydrogen peroxide (1 drachm to a pint of water) may be tried.

If a further test meal be performed after effective treatment, the gastric acidity is often found to have returned.

HÆMATEMESIS AND MELÆNA

Although hæmatemesis is most often due to hæmorrhage from a peptic ulcer, it also results from other conditions. The causes of vomiting of blood are tabulated below :—

1. Vomiting of swallowed blood, *e.g.*, following epistaxis.
2. Bleeding from the œsophagus due to rupture of an œsophageal varix in cirrhosis, or very rarely to hæmorrhage from an œsophageal ulcer or rupture of an aortic aneurysm.
3. Bleeding from the stomach, due to—
   - (*a*) Acute erosion or ulcer.
   - (*b*) Chronic ulcer.
   - (*c*) Carcinoma.
   - (*d*) Irritant poisons, *e.g.*, arsenic.
   - (*e*) Severe gastritis and vomiting, sometimes following alcoholic excess.
   - (*f*) Gastric polyps and adenomata (rare).
4. Bleeding from the duodenum due to an acute or chronic peptic ulcer, with regurgitation into the stomach.
5. Hæmatemesis in certain acute infective diseases, *e.g.*, malaria, yellow fever.
6. Hæmatemesis in diseases of the blood, splenic anæmia, thrombocytopenic purpura, scurvy, leukæmia.

Differential diagnosis of the cause of the hæmorrhage is often easy from the history of the patient. Symptoms, sometimes of long duration, may point to a chronic peptic ulcer. Severe hæmorrhage, however, is not uncommon from an acute ulcer or multiple erosions without any previous

history of dyspepsia. Symptoms of a chronic gastritis, particularly if associated with a history of alcoholism, suggest cirrhosis. In splenic anæmia the much-enlarged spleen and leucopenia render diagnosis easy. In thrombocytopenic purpura or leukæmia there is also evidence of hæmorrhages elsewhere, such as ecchymoses in the skin, epistaxis, or bleeding from the gums.

Sometimes there may be difficulty in differentiating between hæmatemesis and hæmoptysis. The patient's own sensations are a valuable guide, but apart from this, an inspection of the material brought up is generally sufficient. With hæmatemesis there are often remnants of food mixed with the blood ; in hæmoptysis the blood is often frothy and bright red, and blood-streaked sputum continues to be coughed up after the acute hæmoptysis has ceased.

Treatment of Hæmatemesis.—It is unwise to carry out any thorough physical examination until bleeding has ceased for several days, but a careful history should be obtained from the patient and his relatives. Palpation is particularly to be avoided, as it may dislodge clot and lead to further hæmorrhage. The immediate treatment is the same irrespective of whether the hæmorrhage is due to ulcer, cirrhosis, or gastritis.

The first and most important point in the treatment of hæmatemesis is to put the patient at absolute rest ; he should be strictly confined to bed with the head supported by sufficient pillows to ensure comfort ; all visitors or disturbance of any kind must be absolutely forbidden. As soon as possible $\frac{1}{4}$ gr. of morphia must be given hypodermically, and this should be repeated at four- or six-hourly intervals as long as there is restlessness or anxiety, but deep sedation must be avoided. Atropine ($\frac{1}{100}$ gr.) should also be given, as this drug diminishes the secretion of acid and also helps to prevent œdema of the lungs.

As the patient is usually shocked and dehydrated, the mouth is very dry and should be carefully cleaned at frequent intervals to diminish the risk of parotitis. The patient's pulse should be charted hourly and the blood pressure estimated at least thrice daily. A rising pulse and falling blood pressure are indications that bleeding has not ceased, even though there may have been no further hæmatemesis. A blood count should be done and the blood group determined even when the hæmorrhage has not been severe.

Indications for Transfusion.—It is impossible to lay down any hard-and-fast rules as to when blood transfusion is necessary. The percentage of hæmoglobin is of little aid as, especially during the first forty-eight hours, it may remain quite high even though the amount of blood lost has been very large. The hæmoglobin often continues to fall after hæmorrhage has ceased, as the blood volume is made up to normal by fluid from the tissues. The main indications for transfusion are severe shock and collapse, a pulse-rate rising to 120 or above, and a systolic blood pressure falling to 100 mm. or below. Intravenous saline or gum should not be given unless it is impossible to give blood.

It has often been maintained that transfusion may raise the blood pressure and restart hæmorrhage. This is most improbable if blood is given by continuous drip transfusion, and the dangers of giving blood by this method are certainly less than those of withholding transfusion. The blood should be given in amounts of about one pint in four hours. In severe cases many pints may be required. Severe headache, not uncommon in anæmia, is relieved by transfusion.

Operation may be a life-saving measure in patients with a large chronic ulcer where the bleeding is from an eroded vessel. This is most likely to occur in arteriosclerotic patients over fifty years of age. Drip transfusion of many pints is essential as a preoperative measure.

Dietetic Treatment.—Until recent years it was customary to give neither solids nor fluids by mouth until hæmorrhage had ceased for forty-eight hours. As bleeding not infrequently recurred, this policy was often productive of dehydration and inanition, which rectal salines did little to counteract. Meulengracht, believing that many of the deaths from hæmorrhage were due to toxæmia and exhaustion dependent on dehydration and starvation, advocated early feeding of these patients with a practically full diet of high caloric value and ample vitamin content. In Great Britain few physicians follow Meulengracht in allowing meat and fish in the early days of treatment, but there has been an increasing tendency to shorten or abolish the period of initial starvation. Thus Witts advocates on the first day two-hourly feeds of egg and milk with vegetable purée and orange juice. On subsequent days solids such as crustless bread and butter, rusks, and milk puddings are added. Although statistics on gastro-duodenal hæmorrhages are notoriously variable, it would seem that early and adequate feeding has lowered the death-rate and accelerated convalescence.

An antacid such as magnesium trisilicate (15 gr.) should be given between feeds. When bleeding has ceased, 20 minims of a saturated solution of iron and ammonium citrate should be taken thrice daily in milk.

Vitamins B and C are sometimes advisable, *e.g.*, ascorbic acid 500 mg., aneurin 25 mg., nicotinic acid amide 200 mg., and riboflavin 10 mg. daily. These are given intramuscularly.

Melæna.—By melæna is meant sufficient altered blood in the fæces to render them black and tarry in consistency. Following a severe hæmatemesis there is always some degree of melæna. With hæmorrhage from a duodenal, gastro-jejunal, or jejunal ulcer melæna is a more frequent occurrence than is hæmatemesis. When bleeding occurs rapidly the patient may become collapsed and unconscious within a few minutes and may be thought to have had a stroke. The treatment of melæna is similar to that of hæmatemesis. Patients with melæna often have slight pyrexia, probably due to decomposing blood in the intestines.

Prognosis.—Few patients under middle age die as a result of hæmorrhage from a peptic ulcer. When death does occur it is usually due to recurrent or persistent bleeding from an artery exposed in the floor of an ulcer. Without doubt transfusion by the continuous drip method and early feeding have saved many lives.

GASTRIC AND DUODENAL ULCER

Although there are striking differences between gastric and duodenal ulcers, particularly as regards their symptomatology, it is permissible to consider them together, as their pathology and their medical treatment are very similar if not identical. The frequency of peptic ulcer, under which term are included both gastric and duodenal ulcer, appears to have increased very greatly during the past thirty years. To some extent the apparent increase is due to better facilities for diagnosis, but there can be no doubt

that there has also been a real increase, especially in the frequency of duodenal ulcer. Probably an important factor is the general " speeding-up " of life during the present century, with its encroachments on the more placid atmosphere of the Victorian era.

Duodenal ulcer is at least three times more common in males than in females, and gastric ulcer is relatively more frequent in females. As the onset is usually very insidious it is often difficult to be certain at what age the disease really started, but severe symptoms from peptic ulcers are more common above the age of forty than in earlier life. Occasionally there is a striking incidence of duodenal ulcer among the members of a family.

Pathogenesis.—Peptic ulcers only occur in those parts of the alimentary canal in which gastric juice is present. These include the stomach, the first part of the duodenum, and, in cases where a gastro-jejunostomy has been performed, the first few inches of jejunum from the point where it is sutured to the stomach. The natural inference is that the gastric juice or perhaps its hydrochloric acid is in some way responsible. Although gastric juice is unable to digest the normal mucous membrane of the stomach, it is possible that if this becomes devitalised either by trauma, toxins, or local circulatory disturbances digestion of an area of mucous membrane may occur, leading to the formation of an acute ulcer. Although hydrochloric acid is not necessarily present in excess in all cases of peptic ulcer, there is usually some degree of hyperchlorhydria, particularly in duodenal ulcer, and it may be that it is the presence of free hydrochloric acid which prevents the healing of an acute ulcer. Focal infection is probably a less important factor in the genesis of ulcer than it was thought to be in the past. Much stress has recently been laid upon the fact that the symptoms of peptic ulcer frequently follow emotional disturbances and anxiety, and it has been maintained that emotional factors are of prime importance in the development of peptic ulceration and its complications such as hæmorrhage. Although it is undoubtedly true that psychological factors are of great importance, it is doubtful whether they play more than a contributory part in the genesis of ulcer.

Hurst has pointed out that duodenal ulcer is especially common in individuals with the hypertonic type of stomach, which is usually accompanied by hypersecretion of gastric juice and a rapid rate of emptying. The prevalence of this type of stomach in males would help to explain the relative frequency of duodenal ulcer in the male sex.

Symptoms of Gastric Ulcer.—Gastric ulcers may be acute or chronic, and the symptoms of the two conditions are so different that they merit separate descriptions.

1. *Acute Ulcers.*—Little is known of the morbid appearances of acute ulcers, as death rarely occurs. They are usually multiple, and consist of small erosions which, as a rule, do not extend farther than through the mucous membrane and submucous layer. Often they are associated with no symptoms unless erosion of a vessel produces hæmatemesis. Occasionally perforation into the peritoneum may occur. Cases of severe hæmatemesis or perforation without preliminary gastric symptoms are usually due to an acute ulcer. In any case, it is doubtful whether the condition can be diagnosed clinically in the absence of these complications. Acute ulcers are probably an integral part of a chronic gastritis.

2. *Chronic Ulcers.*—The three classical symptoms of chronic gastric

ulcer are pain, vomiting, and hæmatemesis. Needless to say, the last is often absent. The history is extremely important and the diagnosis may often be made from it alone. The onset is usually gradual, and though remissions occur they are seldom of long duration. The pain is situated in the epigastrium, and when the ulcer is in an active condition it occurs with absolute regularity at a fixed time after a meal. In gastric ulcer the onset of the pain is from half an hour to one and a half hours after food; the nearer the ulcer is to the pylorus, the later the onset of pain. The pain usually disappears spontaneously after an hour or two, and is quickly relieved by a dose of alkali such as sodium bicarbonate. Temporary relief is sometimes obtained by taking food, but the pain soon recurs. The patient may have difficulty in getting to sleep owing to pain, but once he has done so is rarely awakened by it. The type of pain varies, but is usually burning in character and may extend through to the back. In most cases nausea accompanies the pain, and vomiting of partially digested food usually gives relief. Only a small proportion of patients have hæmatemesis, but occult blood is practically always found in the fæces when symptoms are present. Some patients with ulcers, whether gastric, duodenal, or gastro-jejunal, seem to have a tendency to repeated hæmorrhages, and in such cases pain is often slight or even absent.

On examining the abdomen there is tenderness on deep pressure in the epigastrium, particularly just to the left of the midline. This is most obvious when there is spontaneous pain at the time of the examination. Rigidity is unusual unless the ulcer is involving the peritoneum, and a palpable tumour is very rare and suggests carcinoma rather than ulcer.

A test meal usually gives little help in the diagnosis unless pyloric obstruction is present. X-ray examination should demonstrate an ulcer in over 90 per cent. of cases. A projection or niche is seen filled with the opaque salt, and when the ulcer is on the lesser curvature an incisura is often visible, due to spasm of the circular muscle fibres.

Symptoms of Duodenal Ulcer.—These are even more typical than those of gastric ulcer. Periods of complete remission of symptoms are more marked than in gastric ulcer, and may last months or even years. Exacerbations are particularly common during the spring and autumn, or when the patient is overworked or worried. The pain in duodenal ulcer occurs at a longer interval after food than in gastric ulcer, often as long as three hours, so that it tends to appear before a meal rather than after one, and is often termed "hunger pain." The appetite is good, but the patient is afraid to eat. Relief is obtained as the result of taking food or alkalis. Vomiting is rare in duodenal ulcer unless cicatrisation is producing pyloric obstruction. The patient is often awakened in the early hours of the morning by pain, and learns for himself that it can be relieved by drinking a glass of milk or eating a biscuit. If an artery be eroded, both hæmatemesis and melæna may occur. Even if there be no visible hæmorrhage, occult blood is found in the fæces. On palpation of the abdomen there is usually deep tenderness in the epigastrium slightly to the right of the midline.

A test meal shows a highly acid resting juice with a rapid rise in acidity during the first hour and sometimes a rather rapid emptying of the stomach. The X-ray diagnosis of duodenal ulcer depends on the demonstration of a deformity of the duodenal cap together with local tenderness on palpation under the fluorescent screen.

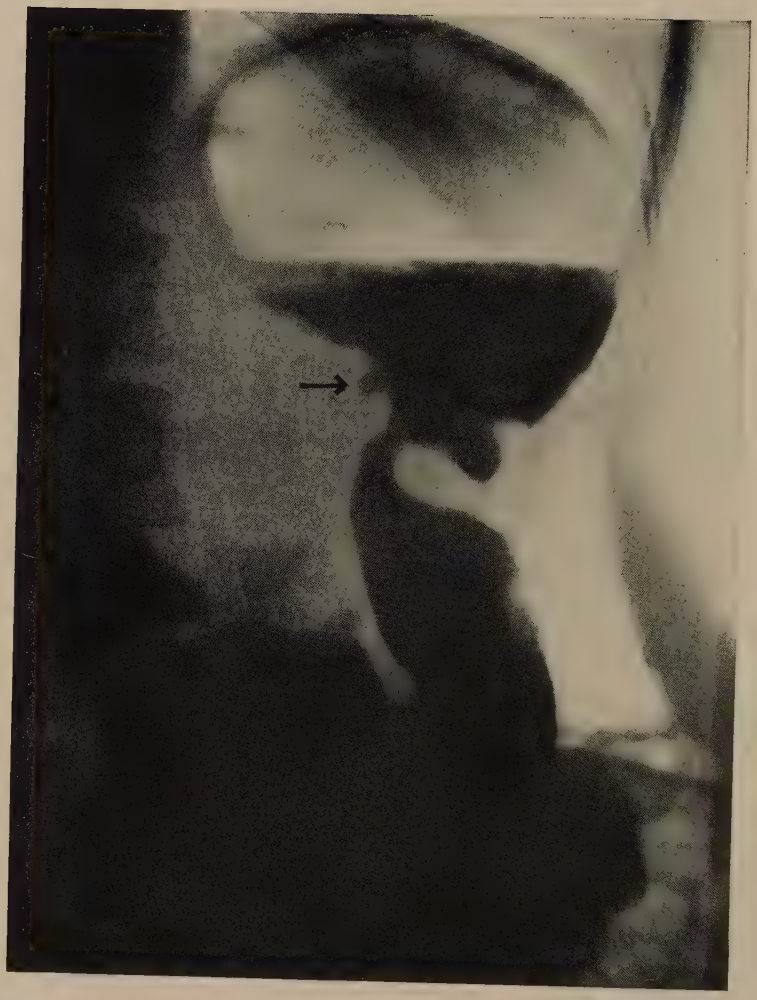

PLATE 14

Hour-glass constriction of stomach. The arrow indicates "niche" of ulcer.
(From plate by Dr P. J. Briggs.)

[*To face page* 307.

Diagnosis of Gastric and Duodenal Ulcer.—A diagnosis has to be made from chronic gastritis, carcinoma of the stomach, and cholecystitis. The points to be considered are set out in tabular form :—

	Gastric Ulcer.	Duodenal Ulcer.	Carcinoma.	Chole-cystitis.	Chronic Gastritis.
Pain—					
Relation to meals	½-1½ hrs.	2-3½ hrs.	Often immediate	Irregular	Usually slight
Relief by food	Uncommon	Very common	Never	Variable	Not relieved
Relief by alkali	Usually	Usually	No relief	Usually not	Not relieved
Appetite	Moderate	Good	Very bad	Variable	Bad in morning
Vomiting	Common	Very rare	Very common	Usually none	In morning
Hæmatemesis	Fairly common	Fairly common	Coffee grounds	None	Rare
Occult blood in fæces	Constant	Constant	Invariable	Sometimes	Sometimes
Acid in test meal	Normal	High	Absent or low	Variable	Usually low
Loss of weight	Slight	Slight	Early and marked	None	None

A further point in cholecystitis is local tenderness on palpation over the gall-bladder, especially when the patient takes a deep inspiration. Although obvious melæna seldom occurs in carcinoma, the presence of occult blood in considerable amount is invariable.

Although the symptoms of chronic peptic ulcers, particularly duodenal, are usually fairly characteristic, there are many occasions on which even a careful consideration of the patient's history and a thorough physical examination fail to point to a diagnosis of a peptic ulcer, which may yet be demonstrated without doubt by X-ray examination. Conversely, X-ray examination may be negative when on clinical grounds an ulcer is almost certainly present.

Complications of Gastric and Duodenal Ulcer

Hæmorrhage and perforation are the two most frequent complications of a peptic ulcer, and they may occur both with acute and chronic ulcers. Hæmatemesis has already been described (*vide* p. 302), and perforation is a surgical condition which is dealt with in textbooks of surgery. Other important complications of chronic ulcers are pyloric stenosis and hour-glass constriction. In addition there are complications which may arise following surgical interference ; these include jejunal and gastro-jejunal ulcers, and gastro-colic fistula.

Hour-glass Constriction.—This rather infrequent complication of a gastric ulcer on the lesser curvature is practically confined to females. The patient gives a history of attacks of indigestion for many years before the more serious symptoms of an hour-glass stomach become manifest. As a result of cicatrisation the stomach becomes divided into an upper and lower pouch with a narrow constriction between the two. When there is serious obstruction to the passage of food the patient vomits almost immediately after a meal and becomes very wasted and cachectic. Abdominal pain is

variable. Patients with advanced hour-glass constriction are usually diagnosed as suffering from carcinoma of the stomach, until the correct diagnosis is established by X-ray examination. The treatment of the condition is surgical.

Apart from hour-glass stomach described above, where there is an organic stricture, there is another condition, sometimes termed spasmodic hour-glass constriction. Here an ulcer on the lesser curvature produces a reflex spasm of the circular muscle fibres opposite it, and this results in an incisura on the greater curvature opposite the site of the ulcer. The condition of spasm is temporary and disappears when the ulcer heals. Spasmodic hour-glass constriction calls for no special treatment apart from that of the ulcer.

Pyloric Stenosis.—The most frequent cause of pyloric stenosis is cicatrisation of a duodenal ulcer. Gastric ulcers rarely produce obstruction of the pylorus, but the condition is common with carcinomata of the pyloric antrum.

Pyloric stenosis can, as a rule, be diagnosed with considerable certainty from the patient's symptoms and the physical signs. The most important symptom is the vomiting of very large quantities of fluid containing food, some of which may be recognised as having been eaten many hours or even days previously. Vomiting is relatively infrequent, seldom more often than once in twenty-four hours, but if the stomach has become very dilated and atonic its contents may be vomited only every two or three days. Pain is generally not a striking feature unless the obstruction is due to a growth. The patient suffers from marked inanition whether the stenosis be due to ulcer or growth. Owing to gastric stasis fermentation occurs and the eructated gas has a foul odour.

On physical examination the abdomen often looks strikingly distended in contrast to the general wasting. The outline of the dilated stomach can usually be seen and waves of peristalsis are visible passing across the abdomen from left to right. There is also a loud succussion splash. The diagnosis is readily confirmed by X-ray examination, which shows very deep and powerful peristaltic waves, which start nearer the cardiac end of the stomach than they normally do. Re-examination after six hours shows most of the opaque meal still remaining in the stomach. A fractional test meal gives important information. With a cicatricial stenosis the amount of free acid rises steadily in the later specimens, but in obstruction due to a carcinoma there is little or no free hydrochloric acid throughout, and much altered blood is present.

Patients with pyloric stenosis due to cicatrisation of an ulcer usually have a history of duodenal symptoms extending over many years. With a carcinomatous obstruction the history is a short one.

With ulcers near the pylorus, whether gastric or duodenal, there may be pylorospasm quite apart from any organic stenosis. With strict dietetic treatment, alkali and atropine, the spasm may disappear. Although there may be definite gastric delay in such cases visible peristalsis is rarely seen, and the amounts vomited are not as great as they are in true pyloric stenosis. Gastro-jejunostomy is inadvisable in pylorospasm unless there is organic stenosis in addition.

Gastric Urœmia.—In pyloric stenosis and sometimes in peptic ulcer, apart from pyloric stenosis, a condition of *alkalosis* may develop, giving

rise to symptoms sometimes described as gastric uræmia. The condition arises from the loss of acid by vomiting and from large doses of alkalis. The danger is increased if the kidneys are inefficient. The symptoms are drowsiness, headache, thirst, hiccups, twitching, and stupor. The blood urea is high, rising to 150 mg. per 100 c.c. or more, and the chlorides are decreased. The urine often contains albumin and casts. Attacks of tetany may occur, but are rare. The condition is a dangerous one, particularly if it remains unrecognised. The administration of alkali must be stopped at once, gastric lavage started, and rectal salines given. In severe cases a continuous drip intravenous saline is required. Operation should be postponed until the blood urea has fallen and symptoms have abated.

Treatment.—Gastro-jejunostomy is most successful in pyloric stenosis due to cicatrisation of a duodenal ulcer. Prior to operation the stomach should be washed out daily. No alkalis should be allowed.

Jejunal and Gastro-jejunal Ulcer.—This is a serious and unfortunately relatively common complication following gastro-jejunostomy, particularly when this operation has been performed on a patient with a high gastric acidity. There is severe pain, usually soon after food, which yields much less readily to treatment than does the pain of a gastric or duodenal ulcer. Melæna is also frequent and may be extremely severe. A majority of jejunal and gastro-jejunal ulcers occur within two years of operation, but they may develop after many years. Prolonged and strict medical treatment is essential, but often further surgical treatment is eventually necessary, which unfortunately is by no means always successful.

Gastro-colic Fistula.—A fistula forms between the stomach and the colon, usually following gastro-jejunal ulceration. The patient becomes very emaciated and suffers from chronic diarrhœa with fæculent eructations. The diagnosis should be confirmed by barium meal and enema. Operative treatment is essential, but the mortality is high.

Treatment of Gastric and Duodenal Ulcer

The most important points in the treatment of peptic ulcer are physical and mental rest. The former can be attained by keeping the patient in bed, though he can be allowed to use the lavatory and bath. Exclusion of business worries and in nervous or irritable patients ½ gr. doses of phenobarbitone twice a day have a good psychological effect. On such a regime, even without special diet or alkalis, symptoms usually are rapidly relieved.

As regards diet there is a wide variation in the practice of physicians, ranging from the strict hourly feed diet of Hurst to the far more liberal diet advocated originally by Meulengracht. Probably as satisfactory as any are two-hourly feeds of non-irritating non-stimulating character, the basis of which is milk and farinaceous food. The calory content must be adequate, certainly not less than 2,000 calories daily, and there must also be sufficient protein and vitamins. Obviously food containing gross "roughage," *e.g.*, cabbage, pips, or skins of fruit, are inadvisable, as are spices, condiments, and meat extracts which induce gastric hypersecretion. Smoking should be entirely forbidden during the course of treatment.

Hourly feeds are practically impossible except in hospital, and it is by no means certain that they have any real advantage over feeds

at two-hourly intervals. The following scheme of diet is usually satisfactory :—

1. *First Week.*—Two-hourly feeds of milk, arrowroot, Benger's food, Horlick's, Ovaltine, cornflour, and the juice of an orange. Sugar may be added to taste.

2. *Second Week.*—Thin white bread and butter with fruit jelly, eggs, custards, milk jellies, potato or vegetable purée can be substituted for some of the feeds.

3. *Third and Subsequent Weeks.*—Boiled or steamed fish, minced chicken, weak tea can be added to the diet of earlier weeks.

Medical Treatment.—Olive oil or cream to diminish gastric secretion, alkalis to neutralise hyperacidity, and atropine as an antispasmodic have long been employed in the treatment of peptic ulcer. Whether they are as important as was formerly imagined is doubtful. Atropine or belladonna has probably little effect in the doses normally employed and may well be omitted during routine treatment. If the patient, however, awakes with pain during the night $\frac{1}{100}$ gr. of atropine hypodermically last thing at night is often helpful. The value of olive oil or cream is doubtful, and in any case they are under present conditions difficult to obtain. The majority of physicians still give alkalis. Probably the two most effective antacids are magnesium trisilicate in 15 gr. doses between feeds and colloidal aluminium hydroxide in 1 to 2 drachm doses. Neither of these drugs produce alkalosis.

Treatment on the lines given above should be adhered to for at least five weeks even though symptoms may have completely disappeared. The effects of treatment may be controlled (i) by X-ray examinations ; (ii) by examination of the stools for occult blood. In the case of a gastric ulcer, the " niche " seen with the X-rays often diminishes in size or even disappears within a month of strict treatment being instituted, and the occult blood, which at the beginning of treatment was well marked, becomes first much reduced and finally is completely absent. With duodenal ulcers, deformities of the duodenal cap persist for many months or years after all symptoms and signs have disappeared. Gastroscopy is also of great value in determining whether a gastric ulcer has healed completely.

In cases of duodenal ulcer which have failed to respond within a few days to medical treatment as outlined above, a continuous milk drip may be tried. A Ryle tube is kept in the stomach for two to three weeks and through it six pints of milk are run by continuous drip during the twenty-four hours.

In addition to dietetic and medicinal treatment, any definite sepsis in the mouth and naso-pharynx should be dealt with, but wholesale extraction of teeth is undesirable.

Peptic ulcers which have healed under treatment are very liable to recur unless the diet and general regime are carefully regulated. Overwork and worry must be avoided and meals must be regular and unhurried. Alcohol in all forms is best avoided for at least a year, and after that period must be taken in only very moderate quantities. Anything in the nature of short drinks before meals should be permanently forbidden. Smoking should be completely stopped for at least six months and oversmoking rigorously avoided later. Fresh fruit with skins and pips are to be avoided, as are condiments such as vinegar and mustard, and highly spiced foods. Regular visits should be paid to a dental surgeon at not more than six-monthly

of those who complain of symptoms referred to the digestive tract. Every practitioner daily encounters patients with symptoms such as abdominal pain or discomfort, distension, flatulence, nausea, vomiting, heartburn, or acid regurgitations, in whom there does not appear to be any evidence of gross organic disease in the stomach or duodenum. In a proportion of such cases the gastric symptoms may be shown to be secondary to local disease elsewhere in the abdomen, for example, in the gall-bladder, and these conditions are described as reflex dyspepsia. In others the failure of digestion appears to be the result of defective nervous control of the secretory and peristaltic functions, and the symptoms produced are termed nervous dyspepsia.

Before proceeding to describe in detail the clinical features of these types of dyspepsia, it is necessary to discuss some of the main symptoms of which these patients complain.

Flatulence.—Most patients use the term "flatulence" to describe the eructation of wind from either the mouth or the bowel, and it is important, when questioning a patient who complains of flatulence, to ascertain the exact nature of the symptom, as gastric flatulence and colonic flatulence are likely to have quite different causes. Most patients with gastric flatulence also complain of sensations of fullness and distension in the upper abdomen or lower part of the chest. The distension produces abdominal discomfort rather than real pain. In the vast majority of cases of gastric flatulence the eructated gas is odourless. When this is not the case the patient is probably suffering from pyloric obstruction or gastro-colic fistula.

Contrary to the belief of most patients who suffer from flatulence, the eructated gas is not a product of abnormal fermentation in the stomach, but is merely air which has been swallowed. The presence of a certain amount of air in the stomach is invariable, but it may be very much increased by the constant swallowing of air (aerophagy). Relief is obtained when the patient eructates, but, unfortunately, repeated attempts to do so result in the swallowing of still more air, some portion of which passes into the small intestine, where it produces loud rumblings and borborygmi, which still further distress and embarrass the patient.

Although flatulence of the gastric type is often no evidence of organic disease, it is important to realise that it is frequently a symptom associated with pathological conditions in the gastro-intestinal tract. Chronic cholecystitis, either with or without gall-stones, almost invariably causes flatulence and distension, which are due in part to aerophagy, but also to disordered gastric motility secondary to inflammation of the gall-bladder. Flatulence is also sometimes a feature of carcinoma of the stomach and of duodenal ulcer; in the latter case it is usually accompanied by epigastric pain of duodenal type. Flatulence also results from hastily bolted meals and defective mastication.

Flatulence is a symptom which varies very much in severity. Patients who eructate like the eruptions of a miniature volcano are less likely to have any underlying organic disease than are those who suffer from more or less silent flatulence. If a patient with severe flatulence is carefully watched, frequent gulping of air can be readily detected. In such cases the mechanism of the condition must be explained to the patient, and particular emphasis be laid on the fact that the regurgitated gas is not the product of fermentation or acidity. Strict injunctions should be given that on no

account should the patient attempt to "bring up wind." Once the habit of aerophagy has been established it becomes a reflex, and the patient has an overwhelming desire to swallow. As this mainly occurs after meals, it is a good plan to instruct the patient to hold a cork between his teeth for half an hour after each meal or whenever he feels distended. This acts as a gag and keeps the mouth open, thereby inhibiting attempts to swallow. Such a procedure, provided it has been preceded by explanation and reassurance, may effect a dramatic cure.

Aerophagy and eructation can be performed voluntarily. In the East, guests at feasts eructate loudly at frequent intervals as a mark of their appreciation of the fare provided, and the guest who does not conform by swallowing adequate amounts of air is thought to be lacking in courtesy.

Acidity.—Many dyspeptics complain of what they term acidity. Usually this is purely an assumption on their part, suggested by the advertisements of patent medicines which purport to remedy the condition. There is, indeed, no evidence that hyperchlorhydria necessarily produces any symptoms, and it is quite common to find that a test meal done on one who considers himself a martyr to acidity may show hypochlorhydria or even complete absence of acid. The only symptom which gives definite evidence of abnormal acidity is acid regurgitation. This is characterised by sudden regurgitation into the throat and mouth of sour, burning fluid. It is not met with very commonly, but may occur in patients with duodenal ulcer.

Heartburn.—The sensation so described is one of burning along the course of the œsophagus. The area in which it may occur ranges along a vertical line extending from the xiphisternum upwards into the neck. The sensation may last for a few minutes only, or sometimes for longer periods. It does not necessarily indicate hyperchlorhydria, and is probably due to tonic contractions in the circular muscles of the œsophagus. Heartburn is a frequent symptom in patients who are overworked, over-anxious, or fatigued. Dietetic readjustments, a holiday, and a little sodium bicarbonate are valuable curative measures.

Waterbrash.—This term is variously used to describe regurgitation of gastric contents or ptyalism (*vide* p. 294).

Abdominal Pain.—It has already been mentioned that pain is not a frequent feature of dyspepsia unless there is a definite lesion such as an ulcer. Sometimes, however, patients complain of hunger pain in the epigastrium. Often this is more a sensation of sinking than actual pain. Whether hunger pain is associated with a duodenal ulcer or not, it is aggravated by worry, fatigue, and cold, and often relieved by relaxation and a holiday. Hunger pain, though most commonly encountered with a duodenal ulcer, also occurs in biliary dyspepsia. Sometimes it is dependent on over-smoking. It is probably produced by excessive peristaltic activity in the pyloric end of the stomach with some degree of pylorospasm. Needless to say, hunger pain should never be regarded as a functional disorder until the most searching investigations have as far as possible ruled out the presence of a duodenal ulcer or other pathological condition.

Nausea and Vomiting.—These symptoms are frequent in patients with organic disease, but also occur with reflex dyspepsia, particularly when this is due to cholecystitis. They may, however, also occur as the result of emotional upsets. Repeated vomiting, particularly immediately after food, is often hysterical in origin. In such cases only a portion of the meal is

vomited, and undernutrition is not striking in relation to the frequency of the vomiting. Psychotherapy and firm handling usually produce a rapid disappearance of symptoms.

Reflex Dyspepsias

The most frequent cause of reflex dyspepsia is chronic cholecystitis, the symptoms of which are described elsewhere (*vide* p. 352). Dyspeptic symptoms are also frequently ascribed, perhaps too frequently, to chronic appendicitis (*vide* p. 327).

Reflex dyspepsia is said to be produced by an epigastric hernia. This is a protrusion of extra-peritoneal fat through the linea alba, which can be felt as a small tender lump in the midline. It rarely causes symptoms, and it is most important before making a diagnosis of dyspepsia due to this cause to exclude other conditions.

Apart from reflex dyspepsia, digestive disturbances are often due to faulty habits. Chief among these are irregular and hastily swallowed meals, physical exercise too soon after food, overeating, or too long intervals without a meal. The symptoms complained of are mostly discomfort and fullness in the epigastrium after a meal and loss of appetite. There is probably a resultant gastritis, and a simple readjustment of the daily routine produces rapid improvement. Such forms of indigestion have been termed by Ryle, "habit dyspepsia."

NERVOUS DYSPEPSIA

At the present time there is a tendency to discourage the employment of the term "nervous dyspepsia" as a diagnosis. While it is true that such a diagnosis should be made with caution and only after a full consideration of the facts in each individual case, there are a large number of patients in whom dyspeptic symptoms can only be explained on the basis of abnormal emotional states. Gastric and intestinal motility depend on the proper functioning of a delicate nervous mechanism, and the same is true of the secretion of the digestive juices. Any factors which upset the nervous mechanism may produce symptoms referred to the gastro-intestinal tract. So common a phrase as "sick with fear" illustrates the familiar fact that fear or anxiety may produce a sensation of nausea or even actual vomiting. Similarly, emotions such as grief or acute anxiety commonly produce anorexia or nausea. Emotion may also disorganise the normal functioning of the intestine or bladder. While it is true that in most normal persons gastro-intestinal upsets due to emotions such as fear, grief, excitement, or anxiety are of comparatively brief duration, there is certainly a well-defined group of patients in whom these factors produce a more lasting effect.

Nervous dyspepsia is one of the most common manifestations of an anxiety state. Often in addition to gastro-intestinal symptoms there may be other complaints, such as palpitation, headaches, lassitude, lack of power of concentration, and insomnia. The symptoms are very variable both in duration and severity. Perhaps the most frequent complaint is flatulence and distension occurring soon after meals. Pain is unusual, though the patient often complains of abdominal discomfort. Anorexia and sometimes nausea are frequent. The anxiety element is usually very obvious and

the patient often fears that he has cancer. Sometimes, however, he is not prepared to admit his fears to the doctor lest he should be thought to be neurotic. In such cases a thorough physical examination, followed by a barium meal, may often effect a remarkable cure.

Probably in all anxiety states the receptivity of the nervous system is increased and patients in this condition become aware of peristaltic movements in stomach and intestine, which in normal persons do not produce any sensations. In addition, owing to the disordered nervous system, there is increased and abnormally vigorous peristalsis, often with considerable aerophagy. Sometimes the condition is aggravated by a great increase in the number of cigarettes smoked, or perhaps by the taking of excessive amounts of alcohol.

A knowledge of the patient's circumstances and environment is of great value. Financial and business worries leading to overwork and exhaustion are potent factors in the production of digestive upsets. The same is true, and even more so, in the case of domestic unhappiness. Marital infelicity, broken-off engagements, unfaithfulness of husband or wife, aged and crotchety parents, illness or deaths of children or loved ones are among the more frequent causes of anxiety states, in which nervous dyspepsia may be the most prominent feature. Perpetual quarrels at meals, so common among ill-assorted couples, are particularly detrimental to the digestion. Alvarez, in his stimulating book on "Nervous Indigestion," quotes the very true words from the seventeenth chapter of Proverbs: "Better is a dry morsel and quietness therewith, than a house full of feasting with strife."

Experimental work both in animals and in man show conclusively that the secretory functions, the blood supply, the motility, and the emptying time of the stomach are profoundly affected by the emotional state of the subject. In a patient with a gastric fistula Wolf and Wolff have shown that emotional conflicts, anxiety, hostility, and resentment cause the gastric mucosa to become intensely red, engorged, and turgid. At the same time there is an increase in the secretion of acid and hypermotility. Normally these features are of short duration and pass off when the emotions become less disturbed. There is, however, some evidence that prolonged periods of emotional upset may induce prolonged hyperfunction in the stomach. Under these circumstances hæmorrhages may occur and minor traumata may produce small erosions, which, if exposed to a high concentration of acid, may result in a chronic peptic ulcer.

It must not be forgotten that patients with nervous dyspepsia are liable to develop an organic lesion, particularly a duodenal ulcer. A careful physical examination and full investigation should be carried out. If negative, this provides additional reassurance both to patient and doctor. Investigations, however, should not be repeated unless fresh developments render these desirable.

The first essential in the treatment of a patient with nervous dyspepsia is to acquire his confidence. On no account should it be suggested that the symptoms are imaginary or exaggerated. In dealing with educated and intelligent patients it is well to stress the fact that the normal movements of the stomach and intestine, and also the secretion of the digestive juices, are all dependent on an adequate nervous control. When the central nervous system is in a state of increased excitability as a result of anxiety, emotion, or overwork and stress, this must react on the nervous mechanism

controlling digestion. If aerophagy is troublesome, as is so often the case, the mechanism by which it occurs can be explained, and the patient is instructed how to avoid swallowing air by restraining his attempts at eructation and keeping his mouth open after meals with a cork. If the dyspepsia is being aggravated by incorrect habits of feeding or by dental sepsis, steps should be taken to readjust the patient's routine, and he should be made to consult his dental surgeon. Sometimes the patient may already be taking purgatives under the impression, derived from advertisements, that they will " clear his system " or " stimulate his liver." If this is so he should be advised to avoid purgative drugs and take small doses of paraffin or petrolagar, if necessary.

In most cases of nervous dyspepsia, reassurance and explanation, combined with rest and a holiday, are of greater value than dieting and drugs. Very often the patient may already have limited the diet to a totally unnecessary degree, and if this is discontinued and a plain ordinary diet instituted, there will be an improvement in the general health. Sometimes patients benefit by taking rather small dry meals with only a little fluid. Excessive tea or coffee should be forbidden. As regards drugs, bromide or phenobarbitone often helps to dull the keen edge of the patient's anxieties. Although nervous dyspepsia is by no means always associated with a high gastric acidity, alkalis are often effective in alleviating the symptoms.

In patients suffering from anxiety neuroses a vicious circle is often established. Dyspeptic symptoms arise as a result of their anxieties, and the digestive disturbance produces still further anxiety. Unfortunately the difficulties, environmental, domestic, or financial, which induce the original anxiety state, are usually beyond the control of the medical attendant, but it is often possible to alleviate the condition by eradicating from the patient's mind the idea that he is suffering from some serious organic ailment.

Visceroptosis.—In the past many patients with nervous dyspepsia were diagnosed as visceroptosis. The stomach, colon, or other organs were thought to be in an abnormally low position in the abdomen, and it was assumed that this supposed misplacement of viscera produced kinks which delayed the passage of intestinal contents; this in turn was assumed to lead to intestinal stasis and autointoxication. Under the influence of such ideas only too many psychoneurotics with vague dyspepsia were in the past subjected to useless and mutilating operations, such as nephropexy, colopexy, gastroplasty, ileo-sigmoidostomy, and colectomy, not to mention appendicectomy for so-called chronic appendicitis.

Fortunately it is now generally recognised that the various abdominal viscera, particularly the stomach and colon, have no fixed anatomical position in the abdomen and that the most extreme degrees of supposed ptosis are consistent with excellent health and robust physique. Consequently the diagnosis of visceroptosis, so popular between the years 1910 and 1925, has now lapsed into well-justified oblivion. This is illustrated by the fact that at Guy's Hospital in the quinquennium 1920-24 the diagnosis of visceroptosis, gastroptosis, and coloptosis were made on 254 in-patients, while during the five years 1935-39 only seven patients were so diagnosed.

In two conditions it is possible that the effects of gravity on the abdominal viscera may produce symptoms. These are chronic duodenal ileus and Dietl's crises.

Chronic Duodenal Ileus.—In this condition there is a narrowing in the

third part of the duodenum where it is crossed by the root of the mesentery. Owing to the constriction the proximal portion of the duodenum is dilated. The diagnosis is primarily made on radiological findings and symptoms are very indefinite. Often there is in addition a duodenal ulcer. Operative procedures designed to relieve the constriction are by no means always successful.

Dietl's Crises.—The kidneys are often readily palpable, especially in asthenic women, and a diagnosis of nephroptosis or "floating kidney" was often made in such cases. Occasionally attacks of renal colic occur in which no stone can be demonstrated. These attacks, which are termed Dietl's crises, are thought to be in some cases due to kinking of the ureter.

On no account should a patient ever be told that an organ is dropped or misplaced, as this is an idea which is very readily accepted by hypochondriacal patients as a rational explanation for a multiplicity of symptoms. The abdominal belts often ordered for so-called visceroptosis give only moral support.

Anorexia Nervosa.—It is a well-recognised fact that after even a short period of fasting there is a loss of appetite, which may sometimes become so complete that the patient loathes even the sight or thought of food. This condition is described as anorexia nervosa and occurs chiefly in young women. Although the patients may be extremely emaciated and cachectic, they nevertheless often lead most active and even restless lives and maintain that they are perfectly fit.

The origin of the anorexia is nearly always psychogenic and not infrequently it follows domestic and emotional conflicts, or it may be a means of escape from a difficult situation. Occasionally it follows on a deliberate reduction of diet owing to fears of obesity. Sometimes, especially in children, refusal to eat starts as an attempt to become a centre of interest. As an example of this condition may be quoted a case who was in Guy's Hospital under the care of Sir Arthur Hurst some years ago. The patient was a girl of seventeen, who for months had been eating practically nothing. On careful questioning it was found that other girls at her school called her a "fat German," as her name was somewhat foreign. Her anorexia had developed in an attempt to diminish her weight, as her name she could not alter. When the position was explained to her she readily consented to eat an ordinary diet and returned to her normal weight and health.

In addition to the anorexia these patients often have amenorrhœa which, in conjunction with the emaciation, sometimes has led to a diagnosis of Simmonds' disease (*vide* p. 224). Injections of hormones, however, are quite useless, and the symptoms disappear if the patient can regain her normal nutrition by returning to a full diet.

Anorexia nervosa is a serious condition, as it renders the patient an easy victim to intercurrent infection. Treatment at home is unsatisfactory. The patient should be kept in bed in hospital and, at any rate to begin with, the doctor must supervise the eating of her meals. A simple explanation to the patient that the illness is due to lack of food is of more immediate value than elaborate psychotherapy. A full mixed diet should be given from the outset, and in addition the patient should be made to take large amounts of glucose. Appetite may be stimulated by soluble insulin given one to two hours before breakfast.

DISEASES OF THE INTESTINES

Physiology of the Intestinal Movements

The small intestine consists of the duodenum, jejunum, and ileum, and is about 22 ft. in length, while the large intestine or colon is about 6 ft. long. The types of peristalsis seen in the small intestine and in the colon are completely different.

The food as it leaves the stomach passes very rapidly through the duodenum and jejunum and gradually slows up in its course through the lower portion of the ileum. In addition to peristaltic waves which sweep the food along the intestine, segmentation movements take place, consisting of localised contractions in the intestine, which help to mix food and digestive juices and bring them in contact with the mucous membrane of the intestinal wall, thereby facilitating processes of absorption.

If the course of a barium meal be traced through the intestines it is found to reach the ileo-cæcal valve in about three and a half hours. Here the barium is held up for a time until the ileo-cæcal sphincter relaxes and peristaltic movements in the terminal coils of the ileum drive the meal through into the cæcum. The passage of the barium into the colon is markedly accelerated during and shortly after the taking of food into the stomach. Thus it would appear that peristalsis in the lower coils of the ileum occurs reflexly as the result of gastric distension, the so-called *gastro-ileal reflex*. Although at an X-ray examination movements of the small intestine are invariably observed, it is extremely rare to see any peristalsis in the large intestine. The explanation of this lies in the fact that colonic peristalsis occurs only at infrequent intervals, probably not more than three or four times a day, and it is therefore unlikely to be observed during the relatively short duration of an X-ray examination. The colonic movements consist of what has been termed "mass peristalsis": the contents of a whole section of the colon move bodily onwards without segmentation through a considerable length of the colon within a period of a few seconds, so that within less than a minute the distribution of a barium meal in the colon may be completely altered. This process of mass peristalsis carries the food residue or fæces around the colon until it reaches the pelvi-rectal flexure, which is a more or less acute angle at the junction of the rectum and pelvic colon. Just as the taking of food produces a reflex stimulation of the movements of the ileum, so it tends to produce mass peristalsis in the colon, the *gastro-colic reflex*.

The act of defæcation is normally initiated by the passage of accumulated fæcal material from the loop of pelvic colon through the pelvi-rectal flexure into the rectum. This is commonly brought about as a reflex result of taking a meal, particularly if the latter be hot or bulky. The distension of the rectum immediately produces a sensation that defæcation is necessary, and the act of defæcation itself occurs partly as the result of reflex contractions in the colon and partly from voluntary relaxation of the anal sphincter, with an increase in the abdominal pressure from voluntary contraction of the abdominal muscles and diaphragm. During defæcation peristalsis occurs throughout the colon, and all its contents, at any rate from the splenic flexure downwards, are driven into the rectum and expelled

through the relaxed anal sphincter. The mucous membrane of the rectum itself is insensitive to tactile stimulation, and the " call to defæcation " is the result of stretching of the muscle fibres of the rectal wall, induced by the entry of fæces into the rectum from the pelvic colon. A similar sensation may be produced by increasing the intrarectal pressure by blowing up a rubber bag placed in its lumen. In normal persons the rectum is empty both after defæcation and until just before the act of defæcation.

CONSTIPATION

What has been said above in reference to the mechanism of defæcation gives us the explanation of that form of constipation, termed by Hurst " dyschezia," which is most commonly met with in practice. By dyschezia is meant an inability to defæcate completely ; even in the most severe cases of this type of constipation there is no delay in the passage of the fæces through the colon until the pelvic colon is reached. The great majority of cases arise from faulty habits regarding defæcation. As has been pointed out, the normal stimulus to defæcation is distension of the rectum, and it must be the personal experience of all that if the " call to defæcation " be neglected for any reason, the sense of discomfort in the neighbourhood of the rectum passes off in the course of quite a short time, and the individual no longer feels any need to empty his bowels. In all probability the feeling again arises after the next meal owing to the rectum becoming further distended, as the result of additional fæces entering it from the pelvic colon. Most cases of dyschezia arise from habitual neglect to respond to the normal stimulus ; this neglect is the result most commonly of laziness or preoccupation with other activities, and is specially liable to occur in childhood. If this habitual neglect is continued over a prolonged period, the warning that defæcation is indicated becomes progressively diminished, until in well-established cases of dyschezia it is possible for the rectum to be continuously distended with fæces without the production of any sensation of discomfort. Only too often after the constipation has lasted for some days the patient takes a powerful purgative, thereby hurrying the passage of the fæces through the parts of the colon in which there is no delay into the pelvic colon and rectum, where it produces so considerable a rise in tension that defæcation is initiated. The bowels having been thoroughly emptied by a purge, the whole baneful process is repeated, and soon the patient gives up all effort to effect an evacuation unless a purge has been taken. Eventually constant stretching of the muscular wall of the rectum and pelvic colon by retained fæces produces a condition of atony and weakness in the muscle fibres themselves, which render recovery from the condition difficult.

Dyschezia is specially liable to occur in young women who work in factories or offices. Often they have a hurried and inadequate breakfast and no time to visit the water-closet before catching train or bus. If a call to defæcation occurs later it is again often neglected as the result of false modesty or a disinclination to leave work. Another potent cause of dyschezia is an inadequate supply of sanitary accommodation in schools or institutions.

For the efficient performance of the act of defæcation there is needed not only the stimulus conveyed by a distended rectum but a forcible contraction of the muscles which raise the intra-abdominal pressure during evacuation.

Consequently, even though there is no delay in the passage of fæces through the colon, dyschezia may result from weakness of the abdominal muscles, the diaphragm, or the muscles of the pelvic floor, all of which come into play during normal defæcation. A sedentary life without any exercise will lead to flabby abdominal muscles ; similarly, overstretching of the abdominal wall as a result of pregnancies or damage to the pelvic floor during labour frequently leads to dyschezia.

Another less frequent cause of constipation is found in local conditions which interfere with the emptying of the rectum. Fissures or inflamed piles by their pain tend to produce spasm of the sphincter and inability to defæcate. Inflammatory conditions of the female generative organs may produce difficulty in defæcation, while the lumen of the rectum or anal canal may obviously be narrowed by such pathological conditions as growths or strictures.

Although the great majority of the cases of constipation commonly met with in practice fall into the class of dyschezia, constipation may also occur in which the passage of the fæces is unduly slow throughout the length of the colon. This is known as colic constipation or colonic stasis and is due to a variety of causes. It may occur as the result of weakness in the muscles of the colonic wall, which are incapable of exerting sufficient force to produce mass peristalsis. This condition is liable to occur in the subjects of chronic diseases and in old age. In other cases there may be spasm of localised areas in the colon leading to what has been termed spastic colitis. This is probably the explanation of the constipation associated with lead-poisoning and sometimes with the excessive use of tobacco. Colic constipation may also occur as the result of pathological conditions in or around the colon, such as growths, strictures due to cicatrisation of ulcers, diverticulitis, or chronic intussusception. In cases of functional nervous disorders, such as neurasthenia and depressive states, constipation is often very troublesome, owing to diminished reflex activity.

Constipation may also be due to a diet inadequate in amount or fluid content, or which contains too little unabsorbable residue. The amount of food actually consumed may be unduly restricted as the result of poverty, deficient appetite, or functional nervous conditions, or it may contain too small an amount of fruit and green vegetables. The passage of the fæces in such cases is not as a rule delayed until the pelvic colon is reached, but owing to inadequate bulk the normal stimulus to defæcation is not produced.

There is a wide variation in normal individuals as regards defæcation. Although a movement of the bowels once every twenty-four hours is usually regarded as normal, there are many people in perfect health who defæcate only once in forty-eight hours ; on the other hand, two or even three motions a day may be simply the result of habit rather than of deranged function. A diagnosis of dyschezia can usually be made on the strength of the history and the constant presence of fæces in the rectum on digital examination. In cases of colonic stasis, an accurate diagnosis usually necessitates the use of X-rays.

Symptoms.—In uncomplicated cases of constipation it is very doubtful whether there is any real absorption of toxins from the retention of fæces in the rectum and pelvic colon. Probably the symptoms complained of are largely the result of auto-suggestion based on advertisements of purgatives. Discomfort is more likely to follow the taking of powerful purgatives, both

from the colic they produce and possibly as the result of toxic absorption from liquid fæces in the colon.

While there can be no doubt that constipation frequently aggravates other diseases such as migraine, epilepsy, asthma, or nephritis, and may in itself produce lassitude, headache, vertigo, anorexia, and many other symptoms, there is no evidence that it is really responsible for the syndrome formerly described as " chronic intestinal stasis."

Treatment of Constipation.—Before attempting to treat a patient with constipation it is essential to arrive at a definite diagnosis of the type of constipation present. Very often a readjustment of the diet with alteration of the daily habits as regards exercise may suffice. In long-standing cases of dyschezia the use of enemata for a considerable period may be necessary, but it is important that the patient should make a real effort to defæcate without artificial aid. The faulty conditions of life which have led to the condition must be explained to the patient, who often, by the time medical advice is sought, is fully persuaded that it is quite impossible for a movement of the bowels to occur without drugs. The volume of the enemata should gradually be reduced, and in most cases after a few weeks of treatment it is found that they can be dispensed with completely. Alternatively small glycerin enemata may be used (2 to 4 drachms of glycerin diluted with an equal volume of water). As it is easier to evacuate semi-solid fæces than the hard scybala common in constipation, liquid paraffin should be taken. In most mild cases this is effective alone if taken properly ; not infrequently patients say that they cannot take paraffin, as it " runs through them " ; on careful inquiry it will usually be discovered that they are taking a single large dose once in the day. As the action of paraffin is purely mechanical, it is important to take it at least twice and preferably thrice shortly after the main meals, as it then is able to get thoroughly mixed with the food throughout the intestinal canal. In order to increase the bulk of the fæces a mucilage such as agar-agar can be given in conjunction with paraffin.

The assumption of a squatting position during the act of defæcation may also be tried, as the pressure of the thighs on the abdomen may help to raise the intra-abdominal pressure.

When constipation is proved to be the result of deficient power or tone in the colon itself, abdominal massage may be useful. If it is due to organic pathological conditions in the colon itself, these must be dealt with.

Although purgative drugs are usually unnecessary for any length of time in constipation, it is often desirable at the beginning of treatment to clear out the intestine. The combination of an enema and 1 oz. of castor oil will usually be efficacious. If purgatives have to be employed over a prolonged period, and paraffin is not satisfactory, an infusion of senna pods may be tried ; five to eight pods are soaked for twenty-four hours in *cold* water, which is then drunk ; the dose can readily be regulated by varying the number of pods.

CHRONIC DIARRHŒA

When a patient complains of diarrhœa lasting for more than a few days the medical attendant must insist upon seeing the stools. Naked-eye examination may reveal obvious blood, mucus, or pus, which necessitates an immediate investigation with the sigmoidoscope and X-ray, if the danger

of overlooking such serious conditions as a growth of the colon or rectum is to be avoided.

Chronic diarrhœa may be due to various causes :—

1. Defective digestive secretions : (*a*) gastrogenous diarrhœa ; (*b*) fatty diarrhœa in pancreatic insufficiency (*vide* p. 358).
2. Organic disease in the intestine : ulcerative colitis, dysentery, growths, tuberculous ulceration.
3. Toxic or infective conditions : uræmia, septicæmia, especially streptococcal, Graves' disease.
4. Nervous diarrhœa.

The diarrhœa associated with the conditions listed under (2) and (3) above is merely a symptom and needs no discussion here. Gastrogenous and nervous diarrhœa are not uncommon.

Gastrogenous Diarrhœa.—Patients with achlorhydria or hypochlorhydria may suffer from a troublesome chronic diarrhœa. The stools are loose, but contain no blood or mucus. The symptoms are as a rule most marked in the mornings. The diarrhœa may be due to impaired gastric digestion and rapid emptying of the stomach. Treatment with hydrochloric acid is often strikingly effective. One drachm of acid. hydrochlor. dil. (B.P.) should be taken in a glass of lemon or orangeade with each meal.

Nervous Diarrhœa.—The satisfactory functioning of the intestinal tract depends on the nervous system. Worry, anxiety, and fear produce over-activity of the gastro-colic reflex and increased intestinal peristalsis, which, though usually a purely transient phenomenon, may sometimes last for long periods, especially in anxiety neuroses. Often this type of diarrhœa is *lienteric*, defæcation occurring immediately after every meal. The symptoms are little affected by diet. In such patients the following mixture is often helpful : tinct. belladonnæ ℥v, tinct. hyoscyami ℥xx, aqua menth. pip. ad ℨss, t.d.s. p.c. Hot drinks are best avoided, but the general nervous condition of the patient needs attention. Reassurance and bromides or phenobarbitone are required. Codeine (½ gr. pill) is often effective and is convenient to carry.

Pseudo-diarrhœa.—Diarrhœa may occur in cases of what is really constipation. Thus with growths of the colon there may be an accumulation of fæces above the stricture, although a certain amount of fluid fæces, often mixed with blood and mucus, are passed at frequent intervals. Similarly intussusception may be characterised by the frequent passage of blood, although obstruction of the bowel is present. Sometimes, even in cases of dyschezia, there may be frequent motions consisting of a few small scybala, and the patient may describe the condition as one of diarrhœa. The error is easily discovered by finding masses of fæces in the rectum.

Undoubtedly some individuals are more liable to attacks of diarrhœa than others, owing to some inherent hyperirritability of the colon. This is often the case after amœbic dysentery. Persons with a tendency to diarrhœa should avoid residence in a tropical climate.

Intestinal Carbohydrate Dyspepsia.—In this condition there is a deficiency of diastase in the intestinal juices, which results in an imperfect digestion of starch. Fermentation occurs in the colon with the production of much carbon dioxide.

Symptoms.—The patient's main complaints are a feeling of abdominal distension and discomfort, borborygmi, and the passage of much flatus. The symptoms are often much aggravated at night, waking the patient and causing insomnia. Pain is unusual, but sometimes there is diarrhœa and colic due to a secondary colospasm. Much relief is experienced after the passage of flatus.

Treatment.—There is no difficulty in the digestion of sugar, and therefore no need for this to be restricted. Free starch, as in flour and bread, is also usually well digested. The starch in root vegetables, rice, and potatoes is, however, enclosed in cellulose envelopes, and it is chiefly in this form that it reaches the cæcum, when the digestion of starch in the small intestine is defective. In intestinal carbohydrate dyspepsia it is therefore important to exclude completely from the diet potatoes, rice, and root vegetables. This is often sufficient to relieve the symptoms. In addition to dietetic restrictions, diastase tablets (5 gr. t.d.s.) may be taken and also 1 to 2 drachms of finely powdered charcoal thrice daily. As a result of treatment the excess of starch in the stools rapidly disappears, and the dietetic restrictions can be gradually relaxed. Potatoes, however, should be avoided permanently.

INTUSSUSCEPTION

In this condition a portion of the intestine, usually the ileum near the ileo-cæcal valve, is invaginated into the lumen of the bowel immediately below. Infants are far more often affected than adults, and in the former the symptoms are acute, whereas in the latter they are usually chronic.

Acute Intussusception in Infants.—Males are chiefly affected and the disease is most common during the first year of life. The victims of acute intussusception are usually healthy, well-nourished infants, but slight gastro-intestinal upsets often immediately precede the onset of intussusception.

Symptoms.—The illness begins with colicky abdominal pain, which causes the child to scream ; soon after the onset, vomiting occurs, but is seldom repeated. After the passage of one or two normal motions, nothing but blood and mucus is passed. On palpation a sausage-shaped tumour is often felt lying transversely across the abdomen with its concavity downwards. This consists of the intussuscepted gut and may ultimately extend round into the left iliac fossa. There is no rigidity except during attacks of pain, but the abdomen may become distended. The pulse is rapid, but the temperature remains subnormal. Unless the condition is relieved by operation, death is almost certain.

Diagnosis.—In infants the passage of pure blood or blood and mucus quite unmixed with fæcal material and with no fæcal odour, is practically diagnostic of intussusception. The typical tumour can often be felt, though occasionally an anæsthetic is necessary to enable it to be recognised. The only conditions with which acute intussusception is likely to be confused are acute colitis or Henoch's purpura, which may indeed sometimes be complicated by intussusception ; in these conditions, however, there is practically always a fæcal odour in the stools even if there be no obvious fæcal material. Moreover, in acute colitis the onset is likely to be more gradual than in intussusception.

Treatment.—Immediate operation is necessary.

Chronic Intussusception.—Intussusception also occurs in adults, more commonly in males than in females ; the condition is usually brought about by the presence of a growth, either innocent or malignant, which forms the apex of the invaginated gut. The symptoms point to an intermittent chronic obstruction, often with blood and mucus in the fæces. Sometimes a palpable mass can be felt in the abdomen ; this may vary in size from time to time and may disappear completely owing to the bowel becoming disinvaginated, only to recur at a later date. Owing to the obstruction, colicky pains occur, and during the exacerbations there may be constipation and vomiting. Sometimes acute obstruction may supervene after a period of intermittent chronic obstruction. Often the condition is mistaken for a growth, and the true diagnosis is not made until laparotomy is performed. Treatment consists in early operation, at which the intussusception is reduced and a careful search made for a cause, such as a polypus or growth.

REGIONAL ENTERO-COLITIS

(*Crohn's Disease*)

Crohn described as "regional ileitis" a condition in which the terminal ileum is found to be thickened, œdematous, and ulcerated. As the cæcum and not infrequently the ascending colon are also involved, Hurst has suggested that the condition should be described as "regional entero-colitis." The ætiology remains obscure, but although histological examination is suggestive of tuberculosis, tubercle bacilli have never been found in the lesions, and the disease is probably inflammatory in origin and non-tuberculous. The lumen of the affected ileum is much narrowed and there is a variable degree of obstruction.

Symptoms are very variable : repeated attacks of colicky pain in the neighbourhood of the umbilicus or in the right iliac fossa ; abdominal distension ; tenderness in the right lower abdomen, where sometimes a sausage-shaped tumour is palpable ; slight pyrexia and polymorphonuclear leucocytosis ; occasionally diarrhœa. Occult blood is present, rarely melæna. There is a tendency in long-standing cases for fistulæ to form between loops of intestine. The symptoms are usually slowly progressive, and a definite diagnosis is seldom made except on the X-ray findings. After a barium meal, repeated examinations of the terminal ileum are made at hourly intervals. Filling defects are seen in the terminal ileum, and the barium shows as a thin irregular linear shadow connecting the dilated coils of ileum to the cæcum. This is known as the " string sign " from its appearance.

Regional entero-colitis is likely to be mistaken for appendicitis, ileo-cæcal tuberculosis, or growth of the cæcum. Excision of the whole of the diseased area is necessary.

APPENDICITIS

Full descriptions of acute appendicitis in all its aspects are available in textbooks of surgery, and here it is proposed to deal only with the condition often described as chronic appendicitis or appendicular dyspepsia.

The symptoms attributed to chronic appendicitis are often vague, variable, and of many months' or even years' duration. Among the more

common are abdominal discomfort or pain, usually epigastric or around the umbilicus, flatulence, and nausea. Sometimes in addition to epigastric discomfort the patient may complain of short attacks of pain in the right iliac fossa. Deep palpation in this region elicits tenderness and sometimes also pain in the epigastrium. The pain differs from that of a peptic ulcer in having a less regular relationship to meals and it is seldom relieved by food or alkalis. It is often aggravated by exercise.

A diagnosis of chronic appendicitis is never justifiable except after a thorough investigation to exclude other conditions such as an ulcer or cholecystitis. The likelihood that the symptoms are due to a nervous dyspepsia must also be carefully considered. Little help is likely to be obtained from X-ray examinations.

During the last twenty years many victims have been sacrificed on the altar of chronic appendicitis. While it must be admitted that sometimes a complete cure is effected by appendicectomy, only too often the patient's symptoms recur within a few months and may lead to further operations for adhesions. Ill-judged appendicectomy is often the prelude to many years of chronic invalidism. On no account should operation ever be undertaken except after the most careful consideration of every aspect, and the patient's desire for operation should never be allowed to influence the decision.

It is important to realise that recurrent attacks of acute appendicitis are entirely different from chronic appendicitis and call for early appendicectomy.

DISEASES OF THE COLON

Methods of Examination

The Sigmoidoscope.—With this instrument it is possible to obtain a clear view of the lower 10 in. of the alimentary canal, and the practical value of this is obvious when it is remembered that this is the portion of the colon which is specially liable to be involved by growths and ulcerative colitis. For a sigmoidoscopic examination it is rarely necessary to give an anæsthetic, either local or general, and with reasonable care there is negligible danger of perforating the bowel. The procedure is uncomfortable rather than painful. Unless the patient is extremely constipated no preparation with purgatives or enemata is required. The latter are liable to produce redness of the mucous membrane, which may be mistaken for inflammation. The examination is made in the knee-elbow position. Before any attempt is made to pass the instrument, a rectal examination should always be made to exclude a growth low down in the rectum. The sigmoidoscope, thoroughly lubricated with vaseline and warmed to body temperature, is inserted gently through the anal canal; when it has passed the anal sphincter, it is pushed in the direction of the sacrum through the first 2 in. of the rectum. The introducer is then withdrawn and the further passage of the instrument is controlled by direct vision. It is most important not to push the instrument forward unless the lumen of the gut is clearly visible. At the upper end of the rectum, 4 in. from the anal canal, the pelvi-rectal flexure is clearly visible and the sigmoidoscope is manipulated around it into the pelvic colon. A carcinoma of the colon may be easily visible through the sigmoidoscope. It bleeds readily and will prevent further passage of the instrument. Swabs for bacteriological cultivation can be taken from ulcers through the lumen

of the sigmoidoscope. A proctoscope is valuable for inspection of the rectum and anal canal.

X-ray Examination of the Colon.—Examination of the colon following a barium meal is not often of great value, except as indicating the rate at which the opaque meal passes round the colon into the rectum. A barium enema is more valuable in the diagnosis of organic disease, particularly cancer, diverticulitis, and ulcerative colitis. After a colon lavage barium is run into the rectum under a low pressure, while the patient is observed under the fluorescent screen. In normal persons the opaque fluid passes readily round the colon as far as the cæcum within a few minutes. A partial stricture of the bowel, such as may result from a carcinoma, will often result in holding up the passage of the enema either indefinitely or for many minutes, and this occurs long before symptoms of intestinal obstruction develop. In addition to the delay in the passage of the opaque salt, there is sometimes a definite deformity or filling defect visible in the shadow cast by the affected region.

Examination of the Fæces.—It is essential to insist on seeing the fæces, as this may reveal the presence of blood, mucus, or pus. This can be confirmed by a microscopical and chemical examination.

CARCINOMA OF THE COLON

Malignant growths of the colon and rectum are fairly common, and may occur at a relatively early age. The most frequent site for the disease is the rectum, but in the colon itself the pelvic portion is most often affected, particularly the last few inches above the pelvi-rectal flexure. The early diagnosis of cancer of the colon and rectum is of the utmost importance, as the growths are often of relatively low malignancy and metastasis is slow.

Symptoms.—These are extremely variable and depend on the situation of the growth and the degree of obstruction which it produces.

1. Sudden onset of acute intestinal obstruction. This is likely to occur with growths of the pelvic colon which encircle the gut.
2. An alteration in the bowel habits in a patient whose bowels previously have been regular. This alteration may be constipation or diarrhœa or more commonly alternation of the two.
3. Visible or occult blood in the fæces. Visible blood is chiefly seen in carcinoma of the rectum or pelvic colon. Occult blood in considerable amount is an almost invariable finding.
4. Abdominal pain. This may be absent but there are often attacks of colicky pain across the lower abdomen or more vague feelings of discomfort or distension. The pain may be definitely related to defæcation.
5. Tenesmus is frequent with growths in or near the rectum.
6. Loss of weight and cachexia only occur late, but sometimes there may be a persistent pyrexia.
7. Hæmorrhoids often develop as a result of a carcinoma of the rectum.

Growths involving the cæcum are less likely to produce obstructive symptoms than are those in the more distal portions of the colon. This is due to the relatively liquid character of the contents of the cæcum. They

may, however, give rise to considerable anæmia from long-continued bleeding. In such cases, although there may be no visible blood in the fæces, occult blood is present in large amounts.

The diarrhœa which is so frequent a feature of carcinoma of the rectum and sigmoid is a pseudo-diarrhœa, in which liquid fæces only, usually containing much visible blood, pus, and mucus, are able to pass the stricture produced by the growth. Above this the colon is loaded with solid fæcal material, and is sometimes palpable in the left iliac fossa. In such cases acute obstruction may develop rapidly.

On physical examination in the early stages little definite information is obtained, unless the growth be palpable on rectal examination. With involvement of the cæcum a mass may be palpable, but growths of the splenic flexure and the pelvic colon are usually too deeply seated to be felt. The rectum is usually found to be empty and ballooned.

Diagnosis.—It is impossible to stress too strongly the importance of making a thorough digital examination of the rectum in every case of piles or where some irregularity of the bowels, whether constipation or diarrhœa, has lasted for more than a fortnight. If nothing be found on rectal examination, the patient must be persuaded to undergo the slight discomfort of a sigmoidoscopic examination. With the adoption of such a procedure as a routine, probably some 50 per cent. or more of growths of the colon would be diagnosed early. The stools must be repeatedly examined for visible or occult blood and a barium enema should also be carried out if sigmoidoscopy is negative.

Other pathological conditions may closely simulate carcinoma of the colon. Most important of these is ulcerative colitis, in which case, however, the diagnosis is nearly always obvious on sigmoidoscopic examination. Diverticulitis, chronic intussusception, regional entero-colitis, hypertrophic cæcal tuberculosis, and amœbic dysentery may all simulate carcinoma of the colon, but can usually be differentiated by the clinical history and radiological findings. Fæcal impaction in the rectum, especially in elderly patients, may give rise to suspicion, but rectal examination reveals the true condition. Attacks of pain may simulate biliary colic.

Treatment.—This is purely surgical, either excision of the growth or colostomy.

Polyposis of the Colon

Single polypi are comparatively common in the colon and rectum, and may cause hæmorrhage or intussusception. They are also liable to become carcinomatous. There is, however, a rare condition, often familial, in which there are multiple polypi throughout the colon. Ulceration and hæmorrhage occur and the stools resemble those of ulcerative colitis. Some of the polypi almost invariably become malignant, and this usually occurs in early adult life. Diagnosis is easy on sigmoidoscopic examination, and a barium enema will show up polypi beyond the reach of the sigmoidoscope as translucent areas (*vide* Plate 18). Bleeding may be considerable and the patient becomes severely anæmic. The outlook as regards development of carcinoma is so bad that colectomy should be advised. Polypi within reach of the sigmoidoscope must be destroyed by diathermy, and the patient should be sigmoidoscoped at six-monthly intervals to detect early any recurrence of polypi. Polyposis also occurs in chronic ulcerative colitis.

PLATE 18

Polyposis of the colon shown after injection of barium and air. (From plate by O. A. Marxer.)

[*To face page* 330.

PLATE 19

Radiograms of ulcerative colitis. The upper plate shows the colon when filled by a barium enema, the lower when the barium has been partially evacuated. (From plate by O. A. Marxer.)

[*To face page* 331.

ULCERATIVE COLITIS

Ulceration of the colon may occur in toxæmic conditions, particularly in uræmia, and it is a constant feature of both amœbic and bacillary dysentery (*vide* pp. 146 and 144). The term " ulcerative colitis " is, however, applied to a well-defined clinical condition in which the colon is inflamed and ulcerated.

Ætiology and Pathology.—The cause or causes of ulcerative colitis remain completely unknown. The disease has been attributed to infection with organisms of the dysenteric type, to Bargen's diplococcus, to excretion of toxins into the colon, to allergy, to vitamin deficiency, and to psychological factors. There is little evidence to support any of the views which have been put forward. The disease is prone to occur in psychologically abnormal people under emotional stress, and relapses not infrequently follow psychic trauma. It is undoubtedly true that muco-membranous colitis (*vide* p. 333) is invariably associated with abnormal types of personality, but these cases rarely if ever develop ulcerative colitis. Most gastro-intestinal diseases are liable to be aggravated by worry and anxiety, but it is difficult to regard them as primarily due to an abnormal psychological state.

With the sigmoidoscope it is possible to obtain a direct view of the mucous membrane of the rectum and lower portion of the pelvic colon throughout all stages of the disease. Before obvious ulcers have formed or after they have healed, the mucous lining of the colon instead of being shiny and moist appears velvety and granular and bleeds readily even with the gentle passage of the sigmoidoscope. This condition, which is similar to that in acute bacillary dysentery, is a diffuse one and may affect the whole of the visible mucous membrane. As the disease progresses necrosis occurs and superficial ulcers are formed which in severe cases become so numerous that practically no mucous membrane remains. In the more chronic cases the submucosa is invaded by a diffuse fibrosis, which eventually reduces the colon to a relatively narrow tube, which when visualised with a barium enema shows a complete lack of the normal haustration. Such a colon with its lack of distensibility and its relatively narrow diameter is incapable of storing its contents, thus accounting for the persistent and intractable diarrhœa (*vide* Plate 19).

In chronic and recurrent ulcerative colitis fibrous strictures may occur and sometimes polypoid adenomata develop, which occasionally undergo carcinomatous changes. Perforation is extremely uncommon. The part of the colon mainly affected is the rectum and pelvic colon, but often the whole organ from the cæcum to the rectum may be involved.

Symptoms.—Even when the onset is apparently acute, careful inquiry often shows that the patient has had at times slight symptoms such as hæmorrhage. Usually the onset is gradual, with diarrhœa as the main symptom. At first the stools are loose, but blood and mucus appear early. As secondary infection of the ulcers occurs pus in the stools becomes very obvious. Fæcal material is nearly always present in contrast to the stools of acute bacillary dysentery. There is sometimes tenesmus and colicky pain, especially immediately before defæcation, but severe abdominal pain is unusual. The general condition of the patient is very variable and probably depends on the extent of involvement of the colon by the ulcerative process. When the colon is widely involved, fever and tachycardia are often prominent

features and the patient's general condition is obviously bad. Even apart from severe hæmorrhage a profound secondary anæmia may develop. Remissions and relapses are frequent, and it is doubtful whether any patient can be said with certainty to be completely and permanently cured. Fistula in ano and anal fissures are distressing complications.

Differential Diagnosis.—Carcinoma coli may produce stools indistinguishable from those of ulcerative colitis. Fortunately sigmoidoscopy rarely leaves the diagnosis in doubt, for in ulcerative colitis the rectum and lower portion of the pelvic colon are almost invariably affected, and if these portions are seen to be normal in a patient who is passing blood and mucus it is almost certain that there is a growth beyond the reach of the sigmoidoscope. Carcinomata of the rectum and pelvi-rectal flexure are readily visible through the instrument. In amœbic dysentery the ulcers are deeper though less extensive and their edges more undermined.

Treatment.—In few diseases is there so great a divergence of views as to treatment. Surgery, medicated colon washouts, anti-dysenteric serum, intestinal antiseptics, vaccines, sulphonamides, vitamins, strange diets, such as apples, all have their advocates. There are, however, two outstanding facts : first, that the earlier treatment is begun the better ; secondly, that prolonged rest in bed and a high calorie diet are of undoubted value.

Diet.—This should be liberal, as the disease lasts for many months and it is important to maintain the nutrition of the patient. Vegetables and fruits which contain much non-absorbable cellulose must be forbidden, but fruit juice is desirable. Finely powdered animal charcoal in doses of 2 drachms or kaolin in ½ oz. doses often helps to reduce distension and relieves discomfort from flatulence.

Colon Washouts.—These are undesirable in acute cases, and even in the more chronic types their value is doubtful. Warm normal saline is preferable to the solutions of tannic acid (1 gr. to 1 oz.) which are often employed.

More valuable than washouts are rectal injections of bismuth subgallate (dermatol), particularly where the rectum and lower pelvic colon is mainly involved. This drug is given in a mucilage made of coreine or isogel flakes (1 drachm of coreine in 4 oz. of water) ; 4 gr. of dermatol are added to each ounce of the mucilage and from 4 to 8 oz. of the emulsion are injected through a soft rubber catheter into the rectum, and retained, if possible, all night. If nocturnal diarrhœa is troublesome 5 to 15 minims of tincture of opium may be added to the rectal injection and ½ to 1 gr. of codeine may be given by mouth.

Blood Transfusion.—This is often of the greatest value, even when the patient is not severely anæmic. It probably acts by improving the resistance of the patient. Several transfusions of half a pint should be given on alternate days. Large doses of iron should also be given.

Surgery.—Ileostomy is undoubtedly sometimes a life-saving operation, particularly in acute cases with grave toxæmia. Following ileostomy some patients put on weight and the colon may even appear to heal. Colectomy has been successfully performed following ileostomy.

Prognosis.—Unfavourable features are a persistently rapid pulse-rate, widespread involvement of the colon, particularly of the cæcum and ascending colon, or the presence of a stricture. The X-ray appearances are of great value. If the colon is small and completely tubular with no haustrations

in any portion, no lasting improvement can be expected. The mortality in hospital is usually about 20 per cent., but if the patients are traced for some years it is considerably higher.

MUCO-MEMBRANOUS COLITIS

Although the term "colitis" ought theoretically to be reserved for definitely inflammatory lesions of the colon, the name mucous colitis or muco-membranous colitis has long been applied to a definite clinical condition characterised by obstinate constipation with mucus in the stools, although there is no inflammatory process comparable to that found in ulcerative colitis.

Mucous colitis is far more frequently seen in females than in males, and usually occurs in early middle life. Its victims are found among the rich rather than the poor, and in addition to abdominal symptoms there is always a marked neurotic element. In the more severe and long-standing cases the intestinal functions acquire an almost complete monopoly of the patient's thoughts and activities, so much so that the character of the fæces becomes the main interest in life.

The characteristic symptoms of muco-membranous colitis are constipation, the passage of mucus in the stools, and sometimes abdominal pain. The mucus may be excreted in unformed masses, but more frequently it occurs in the form of long strips, somewhat suggestive of a tape-worm. In severe cases there are complete casts of the colon which may be many inches in length. Microscopical examination of the mucus shows the presence in it of a few desquamated epithelial cells, but no pus cells. The fæces themselves are hard and scybalous unless the patient has taken violent purges, which may induce a transient attack of diarrhœa. The mucus is secreted by the glands of the colonic mucous membrane, under the combined influence of a hyper-irritable nervous system and an obstinate constipation. Owing to the unfortunate mental attitude of the patient, the symptoms are grossly exaggerated and the passage of mucus causes the most intense mental agitation, even though it may be accompanied by no other symptoms. Not infrequently there is in addition a spastic condition of the colon, which may often be felt on palpation to be firmly contracted. Such spasticity is often the cause of abdominal pain, which is aggravated by the taking of powerful purges. The most frequent site for pain is down the left side of the abdomen and in the left iliac fossa. Sigmoidoscopic examination shows a normal mucous membrane, but spasm of the circular muscle of the gut throws the mucous membrane into folds and tends to obliterate the lumen. In chronic cases where powerful purgatives have been employed there may be some congestion and slight bleeding.

The treatment of severe cases of muco-membranous colitis is one of the most trying tasks that beset the medical practitioner. Only too often the patient has already tried every conceivable line of treatment, and visits her doctor with an unalterable determination not to get well. In addition she is often regarded as a heroic martyr to her health by anxious relatives. In consequence the outlook is most unfavourable.

An attempt must be made to deal with the constipation, and at the beginning of treatment it is important to get the bowels completely emptied,

an object which is best attained by the combined use of castor oil and enemata. Subsequently copious doses of liquid paraffin should prevent a fresh accumulation of fæces, and in addition rectal injections of warm olive oil may be given at night and retained till the morning. Where the constipation can be shown to be due to stasis in the upper part of the colon, the action of the paraffin may be reinforced by taking an infusion of senna pods, but all more powerful purgatives must be absolutely prohibited.

As the colon is abnormally irritable the diet should consist of foods which leave little residue, and uncooked green vegetables or fruits with skins or pips must be avoided. The inclusion of coarse articles of food such as bran, which act as a stimulant to the peristalsis of a normal intestine, is likely to produce an increase in the secretion of mucus.

When there is spasticity of the colon a useful prescription is tinct. belladonnæ ℥v, tinct. hyoscyami ℥xx, aq. menth. pip. ad ℨss. t.d.s. p.c. Smoking should be forbidden. Vaccines are of no value, while all forms of operation, such as colopexy, short circuit, or colectomy are disastrous.

Mucous colitis is treated by colon washouts at spas, such as Plombières, Harrogate, and Buxton. On the whole it is best to avoid anything in the nature of regular enemata or colon washouts, as such treatment tends to make the patient concentrate her attention on her colon. Such successes as are obtained by spa treatment are probably due not so much to the special properties of the waters as to the regularity of the life and the expectation of cure on the part of the patient, which is fostered by the whole atmosphere of treatment.

Anything which will serve to distract the patient's attention from her complaint is of value. Unfortunately, most of those afflicted with the disease are blessed, or perhaps cursed, with sufficient money to relieve them of any need to earn a living. Plenty of open air and exercise are indicated, but care must be taken to avoid cold, particularly upon the abdomen.

Proctalgia Fugax.—This term has been used to describe paroxysmal attacks of pain in the rectum. It is probably due to painful spasm of the levator ani muscles. The attacks usually wake the patient and last about five minutes. They can sometimes be relieved by firm digital pressure on the anal canal. Physical examination is negative.

DIVERTICULITIS

Both at autopsy and in X-ray examinations of the colon small diverticula are found in about 5 to 10 per cent. of persons over middle age. These diverticula are most frequently encountered in the pelvic colon, though they may occur throughout its length. They are more common in the male sex, but there is little evidence that they are specially frequent in the obese. In many cases they appear to cause no symptoms, and the condition has been termed by Spriggs "diverticulosis." The exact mechanism by which diverticula are produced is uncertain, but there is no evidence that they are due to constipation.

If the openings of diverticula become narrow, fæcal material may stagnate in the pouches and infection supervenes. This gives rise to symptoms, and the condition is then described as diverticulitis. The inflammatory changes

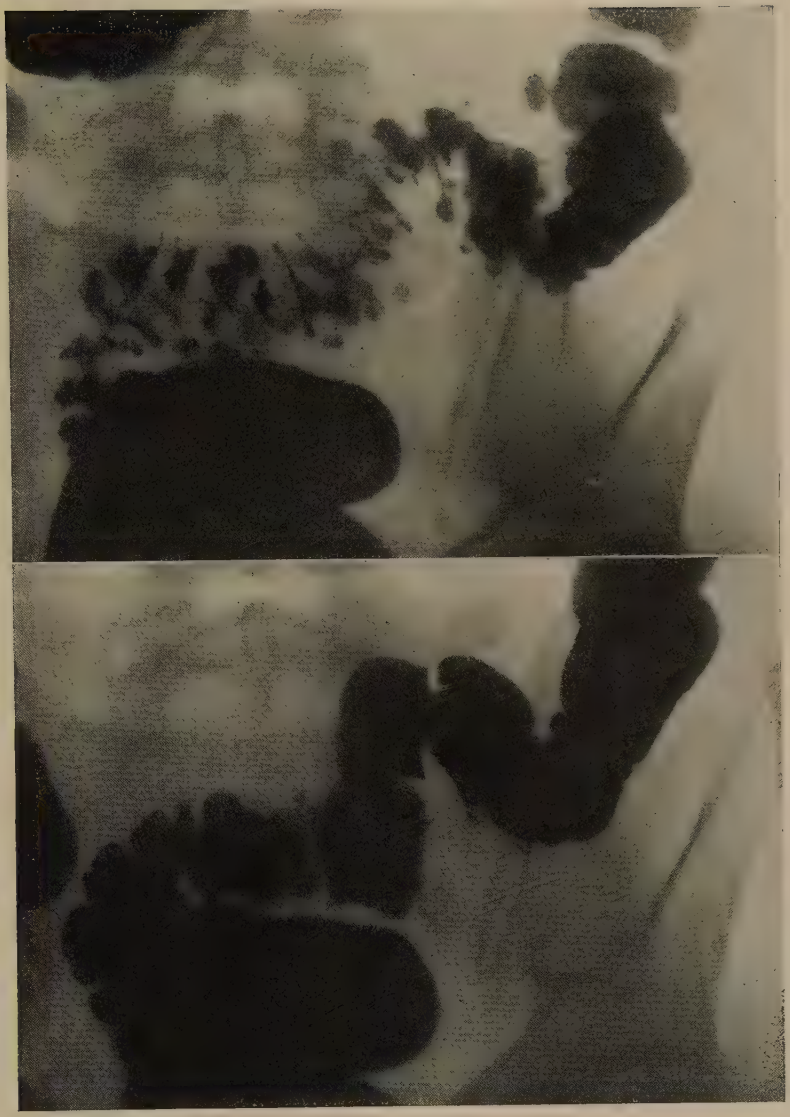

PLATE 20

Diverticulitis of colon. The X-rays were taken before and after treatment. (From plate by O. A. Marxer.)

[*To face page* 334.

lead to thickening of the affected area of the colon, which becomes adherent to surrounding structures. Sometimes perforation may occur with the formation of localised abscesses, or adhesions to the bladder may cause urinary symptoms or even a colo-vesical fistula.

Symptoms.—Abdominal symptoms vary according as the inflammatory process is acute or chronic. In the acute form acute appendicitis may be simulated, except that the pain, tenderness, and rigidity are in the left iliac fossa. As a rule the acute process subsides, sometimes with the formation of an abscess. Acute perforation is very rare.

In the more usual chronic types of diverticulitis the symptoms may occur intermittently for many years with exacerbations and remissions. Abdominal pain, chiefly in the left lower abdomen, is the most frequent complaint. It is often aggravated by defæcation. The bowels tend to be constipated or irregular, but diarrhœa is unusual. Visible blood in the stools is uncommon. Occult blood, however, particularly hæmatoporphyrin, is often present. Dysuria may indicate adhesion of the inflamed diverticula to the bladder. There is usually tenderness in the left iliac fossa and sometimes a sausage-shaped tumour may be palpable. Occasionally obstruction develops, but this is usually gradual in onset. During the acute or subacute phases of the disease there may be fever and a polymorphonuclear leucocytosis.

Localised abscesses may form large abdominal tumours and may burst into the bladder, vagina, or colon.

Diagnosis.—This can usually be settled by a barium enema, which may demonstrate the diverticula filled with barium. It is important to remember that the mere discovery of diverticula does not necessarily mean that the patient is suffering from diverticulitis. With carcinoma of the colon there is more likely to be diarrhœa or obvious blood and mucus in the stools, and a barium enema will show a localised filling defect. Moreover, in most cases of diverticulitis the long history makes a growth of the colon improbable.

Treatment.—Surgery is rarely necessary. In most cases rest in bed, a low-residue diet, plenty of paraffin, and saline colon washouts may relieve the symptoms. In addition, a mixture containing tincture of belladonna ℥v and tincture of hyoscyamus ℥xxx may relieve spasm. A few ounces of warm liquid paraffin should be injected into the rectum and retained overnight.

HIRSCHSPRUNG'S DISEASE

This interesting though rare condition consists of great dilatation and hypertrophy of the colon, particularly in its distal portions. It is also known as megacolon and idiopathic dilatation of the colon.

Hirschsprung's disease is usually congenital, but it sometimes is first discovered in adult life. Possibly the condition is analogous to achalasia of the cardia (*vide* p. 297), being due to a failure of the anal sphincter to relax. This obstructs the evacuation of the colon, which consequently becomes enormously dilated and hypertrophied.

The symptoms are very variable. In adults they may be few, apart from constipation and colonic flatulence. In early life they are often severe; intractable constipation, abdominal distension, malnutrition, and sometimes

obstruction. The enormous dilatation of the splenic flexure may push the diaphragm upwards and produce dyspnœa. Occasionally patients complain of severe attacks of colicky pain simulating obstruction, but as a rule these pass off spontaneously.

On examination the abdomen is distended and the outline of portions of the dilated colon is obvious. The diagnosis is readily confirmed by a barium enema. Between 6 and 8 pints of the emulsion are required to fill the dilated colon, as compared with about 2 pints for the normal colon.

Treatment.—If the patient has been constipated for a long period and the rectum is filled with scybala, it may be necessary to give an anæsthetic and remove the contents manually or with a spoon. A wide bore tube must be manipulated into the colon and its contents thoroughly washed out. Once evacuated, the colon must not be allowed to refill. This object can sometimes be attained by daily dilatation of the anal sphincter with a tapered bougie, which is kept in position for fifteen minutes before attempts at defæcation. Often daily saline washouts are necessary. Lumbar sympathectomy rarely produces good results, but spinal anæsthesia often relieves symptoms, and the improvement persists for long periods.

Megacolon in adults often causes little disability, and is consistent with continued good health and activity. In children the outlook is usually said to be unfavourable, but often this is not the case.

J. J. Conybeare.

DISEASES OF THE LIVER, GALL-BLADDER, PANCREAS, AND PERITONEUM

DISEASES OF THE LIVER

The Estimation of Hepatic Efficiency

THE remarkable regenerative power of the liver and the wide margin of safety which it possesses makes it difficult to assess the degree of damage from any cause. In the presence of obvious structural damage the functional ability of the liver may be unimpaired as measured by any single test. The efficiency of the many functions has necessarily to be gauged by a careful survey of the symptoms and signs in conjunction with a variety of observations and tests, conclusions being drawn from the combined data.

The presence of urobilin in the urine is the most delicate indication of parenchymal inefficiency. The van den Bergh test and the icterus index are used in measuring the degree of jaundice, a common sign of liver disease, though they do not reveal the cause. The bromsulphalein test measures the liver's ability to excrete a foreign dye substance, but is not helpful in differential diagnosis nor of much practical value. Inability of the liver to form the normal amount of prothrombin, in spite of an adequate supply of vitamin K, is a sign of severe damage. This is measured by the clotting time of blood plasma under certain fixed conditions, *i.e.*, prothrombin time.

The concentration of plasma proteins is influenced by the liver. In certain forms of liver damage the plasma albumin decreases and the globulin increases. This alteration in the ratio of the plasma proteins and the presence of abnormal globulins may occur in cases of infective hepatitis and in early cirrhosis, and is the basis for such tests as : (i) the cephalin-cholesterol flocculation test ; (ii) the thymol turbidity : (iii) the Takata-Ara test. These may be valuable in disclosing liver disease in the absence of jaundice.

The ability of the liver to detoxify certain substances can be measured by the hippuric acid excretion test. Sodium benzoate is given either by mouth or intravenously, and the liver's efficiency in conjugating it with amino-acetic acid to form hippuric acid is demonstrated by the appearance of hippuric acid in the urine during the next few hours.

The galactose test is useful in measuring the capacity of the liver to convert sugars into glycogen. Galactose is practically not utilisable by any other tissue, and if present in the circulation is passed in the urine. Under fasting conditions, if 40 gm. of pure galactose are administered by mouth in 250 to 500 c.c. of water, then in the next five hours none or less than 1 gm. of sugar is excreted normally in the urine. Any appreciable inefficiency of all the liver cells is shown by there being at least 2 gm., and when severe more than 3 gm. of sugar in the urine during the whole five-hour period.

Cases of toxic and infective hepatic jaundice show the greatest glycosuria, while in obstructive jaundice (early or late stage) the test gives a normal result.

The phosphatase content of the blood is usually raised in obstructive jaundice. Though both the galactose excretion and the blood phosphatase are of assistance, neither is an infallible guide in the differential diagnosis between obstructive and parenchymal jaundice (*q.v.*).

Jaundice (*Icterus*)

Jaundice means the visible staining of the tissues by bile pigment. It appears when the plasma-bilirubin reaches 2 mg. per cent. as measured by such methods as the icterus index and the more specific van den Bergh test. If increased for any length of time the deposition of bile pigment in the tissues becomes visible in the conjunctivæ, mucous membranes, the skin of the face, and finally of the whole body. Bilirubin is formed from hæmoglobin by the cells of the reticulo-endothelial system, which are widely distributed throughout the interstitial and perivascular tissues of the body. Though the Küpffer cells belong to this " system," yet they form but a small portion of it. The role of the liver, therefore, as a site for the production of bilirubin is relatively negligible. The polygonal cells which make up its main mass are concerned with the removal of bilirubin from the blood, its conversion, and excretion into the bile canaliculi. In hepatic diseases this selection and excretion of bile pigment is often disturbed, so that the bilirubin content of the blood plasma may rise and may be changed in quality as well. Thus jaundice may be due either to mechanical defects in the outflow of bile from obstruction of the ducts, or to morbid processes in the liver cells themselves, or more rarely to increased production of bilirubin due to excessive hæmolysis of red cells. These causes may be classified as : (i) obstructive hepatic jaundice ; (ii) toxic or infective hepatic jaundice ; (iii) hæmolytic jaundice.

Obstructive Jaundice

The causes of obstruction of the common bile duct may be tabulated as follows :—

1. Causes within the duct, *e.g.*, gall-stones, parasites (these *very* rarely).
2. Causes in the wall of the duct, *e.g.*, carcinoma of the duct, congenital stenosis, trauma (usually post-operative cicatrisation).
3. Causes outside the duct, *e.g.*, carcinoma of the pancreas, chronic pancreatitis, enlarged glands in the portal fissure.

Depending on the cause, obstructive jaundice may be partial, complete, or intermittent. As soon as the flow is impeded, the pressure rises in the bile ducts, and absorption of bile into the blood stream results.

The Signs and Symptoms of Obstructive Jaundice.—About twenty-four hours after the onset of obstruction, jaundice becomes visible in the conjunctivæ and mucous membrane of the hard palate ; later the skin of the face, neck, and body becomes stained. In artificial light, slight jaundice is easily missed, while, on the other hand, fat in the lower part of the sclera and in the conjunctivæ may be mistaken for jaundice. At first the colour is light yellow, but gradually deepens until in chronic cases the whole skin

becomes of a dark green or greenish-black hue. Bile pigment and bile salts are present early in the blood plasma and in the urine, which becomes noticeably dark in colour. Casts and albumin are often present. With the exclusion of bile from the intestine, the stools become greyish-white in colour, putty-like and bulky, owing to the large amount of fatty acids and undigested fat. The absence of bile acids from the intestine so diminishes the absorption of fat that the quantity in the stools may rise to nearly 80 per cent. instead of the normal 20 per cent. The liver is usually enlarged, but not tender unless the dilated intrahepatic bile ducts have become infected. The gall-bladder may be distended and palpable when the common duct is obstructed by malignant disease. When, however, obstruction is due to a gall-stone, the gall-bladder also contains stones and cannot become distended owing to thickening and fibrosis of its wall. This is known as Courvoisier's law.

If jaundice persists, xanthomata (cholesterin tophi) may appear anywhere, most commonly on the eyelids, hands, and feet. Telangiectases often develop on the forearms, hands, face, and in the mouth. Operative procedures are dangerous owing to the prolonged bleeding time, which results from a lowering of the level of plasma prothrombin. This is due to vitamin K deficiency, which develops from poor absorption when bile is excluded from the intestine. This vitamin should be given parenterally as a pre-operative measure to patients with jaundice. Unlike acholuric jaundice, the red cells have an increased resistance to hypotonic saline. In the absence of complicating infection, leucocytosis is usually absent. The blood phosphatase and cholesterol are increased, and the van den Bergh test gives a direct positive reaction. The pulse is usually said to be slow, but this is seldom the case.

Few symptoms are caused by jaundice itself. The pruritus, sometimes extremely severe, may be pre-icteric, and is perhaps due to bile salts or hypercholesterolæmia. Xanthopsia, or yellow vision, which is very rare, is not dependent on the degree of jaundice, but is probably a toxic effect on the retina. Irritability, mental dullness, and depression are common. Progressive liver insufficiency leads to serious toxic symptoms, such as delirium and convulsions, or a typhoid state with dry tongue, hiccough, tachycardia, epistaxis, hæmatemesis, and slight fever. This stupor increases to coma and finally death. Such a condition is termed cholæmia, indicating the failure, collectively, of the functions of the liver from this secondary biliary cirrhosis.

Toxic or Infective Jaundice

Jaundice is occasionally seen as a complication in severe infective conditions such as pyæmia, pneumonia, or typhus. Certain poisons such as arseniuretted hydrogen, arsenic, chloroform, T.N.T., phosphorus, carbon tetrachloride, and poisonous mushrooms (*Amanita phalloides*) cause this form of jaundice. It is also the most prominent feature in virus hepatitis (see Infective Hepatitis), Weil's disease (*q.v.*), and in acute hepatic necrosis. In all these conditions there is no biliary obstruction, and the jaundice is the result of intrinsic cellular damage. Fatty infiltration of the liver is prone to occur when there is any damage to its cells.

In cirrhosis of the liver (*q.v.*), though jaundice is absent or slight, cellular damage of this toxic or infective type proceeds in varying proportions of

degeneration and regeneration, but the formation of fibrous tissue in the portal areas is an additional and characteristic feature.

Forms of Acute Primary Hepatitis

1. Catarrhal jaundice.
2. Infective hepatitis.
3. Homologous serum jaundice.
4. Acute hepatic necrosis (acute yellow atrophy).

Ætiology and Pathology.—Apart from the degree of damage, no biochemical or pathological variation distinguishes these conditions. The infective agents causing them appear to be various strains of viruses which may be closely related. They are resistant to freezing and drying for months, withstand heat to 56° C. for one hour, and are filterable. Infection takes place by mouth, or can be introduced subcutaneously or intravenously. Acute hepatic necrosis can also be caused by certain poisons (see Toxic and Infective Jaundice above).

The liver cells show changes ranging from mild inflammation to widespread disintegration and necrosis. Areas of lymphocytic infiltration are seen in the periphery of the lobules and periportal regions and sometimes in the body of the lobule. In the most severe cases autolytic necrosis is widespread, and the liver shrinks, is flabby, yellowish-green in colour, mottled from subcapsular hæmorrhages, and the capsule is wrinkled (acute yellow atrophy). When necrosis is less acute the areas of regeneration are more marked.

1. **Catarrhal Jaundice.**—Catarrhal jaundice is a mild acute hepatitis, and is common especially during adolescence and up to early middle life. Sometimes it occurs in small or localised epidemics. One attack confers immunity, but not to other virus infections of the liver.

Symptoms and Signs.—Slight gastric disturbances with loss of appetite, a feeling of fullness in the epigastrium, nausea, and vomiting may initiate the attack. These symptoms, with slight fever (100° to 101°), malaise, and lassitude, may precede the jaundice for some days. Rarely, particularly when it occurs in old people, there may be no gastric symptoms, and the gradual appearance of the jaundice is the first indication of the disease. Itching of the skin may precede or accompany the jaundice and can be distressingly severe. The urine shows bile pigment early and the stools become clay-coloured. The other symptoms usually abate with the appearance of jaundice. The liver is usually enlarged and may be slightly tender. The spleen is sometimes easily palpable. Mental depression and drowsiness may be present. Colour may return to the stools and the jaundice begin to fade in a week, but a duration of three to four weeks or even longer is more common. The return of bile pigment to the stools is the first sign of recovery. Urobilinuria is present when the stools contain bile pigment, disappearing gradually as the liver cells recover.

2. **Infective Hepatitis.**—During the late war, and in previous wars, epidemics of infective hepatitis were common among the armed forces. Though due to a virus infection not one strain alone is responsible for all the cases nor is the virus the same as that causing the common catarrhal jaundice, even though the mild forms are indistinguishable from that disease in symptomatology and course. When epidemics take place transmission

is probably from excretory products, and infection takes place by mouth. The incubation period appears to be from fifteen to thirty-four days. In sporadic cases a virus causing infective hepatitis may have been conveyed in solutions given subcutaneously or intravenously.

Symptoms and Signs.—A prodromal stage may precede the appearance of jaundice by a few days to several weeks. It often begins mildly as in catarrhal jaundice or as a more severe illness with a greater degree of malaise, headache, lassitude, anorexia, abdominal discomfort such as distension, intestinal cramps, soreness in the right upper quadrant, general body aching, chilliness, and fever of 100° to 103°. There may be diarrhœa and nausea and vomiting. Enlarged lymph nodes may be present in the neck. The liver is usually tender, but not necessarily much enlarged. The spleen may be felt in a few cases. At this stage large amounts of urobilinogen will be present in the urine, the serum bilirubin may be increased, van den Bergh's diazo test showing a direct reaction and the flocculation liver function tests show abnormal results. Gradual subsidence of the symptoms then may occur for five to ten days with little or no fever until the second stage is ushered in by an exacerbation of all the previous symptoms as jaundice appears. Fever is usually milder. The liver may enlarge further and be quite tender. The spleen is sometimes easily palpable. Lassitude and somnolence, intestinal cramps, occasional loose stools, and nausea and vomiting may be distressing. A leucopenia is a usual finding. This secondary or icteric stage may last two to four weeks, but certain cases may continue for eight to twelve weeks. The disappearance of jaundice does not necessarily indicate recovery. In a very small number no jaundice occurs, though the clinical course is otherwise similar. The majority of cases do well. A small percentage are fatal, either within a relatively short time from a widespread necrosis of the liver or after two to three months from a long persistent infection with gradual failure of liver function.

3. **Homologous Serum Jaundice.**—This is a form of infective hepatitis, mentioned above, where the virus appears to have been conveyed in any material in which blood plasma, serum, or whole blood has been used and obtained from donors not suffering from any illness. In this war the unsuspected presence of the icterogenic virus in pooled blood was, and still is, an important problem. Vaccines may be a source. Imperfectly sterilised syringes and needles can also be responsible, and it is probable that some of the cases of hepatitis following arsphenamine therapy were of this nature. The incubation period is long—from fifty-four to one hundred and eighty days.

4. **Acute Hepatic Necrosis (Acute Yellow Atrophy).**—This may occur in the most severe types of infective hepatitis, or as the result of certain poisons (*vide* p. 339). However, there may be no obvious cause. When this is the case the most frequent associated factor is pregnancy. The onset, with the prodromal stage, is similar to that described under infective hepatitis, but the second stage is marked by extreme toxæmia, weakness, prostration, headache, irritability, delirium, and torpor. The jaundice and vomiting become more severe because of renal insufficiency. The pulse is feeble and rapid, the tongue dry and coated. Subcutaneous and submucous hæmorrhages are common from lack of prothrombin production. Though at first the liver may be enlarged and tender, there is soon a rapid diminution in size, and the hepatic dullness may disappear as the necrotic organ softens,

shrinks, and falls back allowing the intestine to overlie it. Occasionally severe pain occurs when patches of further necrosis take place suddenly. The spleen sometimes becomes palpable. The urine is diminished in amount and contains bile pigment, albumin, and casts. Drowsiness increases to stupor and coma until death occurs.

Hæmolytic Jaundice

This is the term applied to any jaundice dependent upon the excessive destruction of red blood cells with the liberation of hæmoglobin and its transformation into bilirubin by the cells of the reticulo-endothelial system. This change takes place independently of the liver, and the hepatic cells are able to excrete the excess bilirubin brought to them up to a certain point, but beyond this are unable to do so, and jaundice results. The jaundice occurring in acholuric jaundice is of this type (*vide* p. 265).

The Diagnosis between Obstructive and Toxic or Infective Hepatic Jaundice

This problem may be difficult, since the prolonged absence of bile pigment from the stools is consistent with either type. A careful history of the onset of any ill-health and the exact sequence of symptoms and signs is important. The objective is to make clear, if possible, whether the earliest symptoms were those of liver dysfunction on the one hand or, on the other hand, whether they indicate disease outside the liver itself, the jaundice being incidental to the interference with the patency of the common duct. Obstruction causes, apart from the jaundice, symptoms and signs of passive congestion of the bile canaliculi throughout the liver, with or without infection. Symptoms and signs of damage to the parenchymal cells of the liver come relatively late in the sequence of events. In hepatic jaundice symptoms of liver disease (anorexia, malaise, lassitude, nausea, vomiting, etc.) precede the clay-coloured stools, whereas in obstructive jaundice the onset may be uneventful, as in many cases of carcinoma of the head of the pancreas, or marked by biliary colic in the case of common duct stone. Also in hepatic jaundice the enlarged liver may be tender quite early and the spleen soon be palpable, while in obstructive jaundice the enlarged liver will not be as tender until cholangitic infection makes it so. The secondary biliary cirrhosis will then be accompanied by splenic enlargement. Further misleading points are the facts that an acute hepatitis may cause pain suggesting that of mild biliary colic, and that a stone in the common duct may sometimes, though rarely, occur without pain, or a history of pain. In addition, patients with carcinoma of the pancreas may have pain.

Certain tests sometimes assist in the diagnosis. The blood phosphatase is elevated in obstructive jaundice, and the galactose tolerance test remains normal even when the obstruction has been of long duration. In hepatic jaundice the galactose tolerance is impaired. Lowered serum albumin with increased serum globulin occurs characteristically in hepatic jaundice and gives positive results to such tests as the cephalin-flocculation and Takata-Ara.

In some cases, even after careful observation for many weeks, the diagnosis may remain uncertain, and an exploratory laparotomy should be considered.

The Treatment of Acute and Subacute Parenchymal Disease of the Liver

Adequate rest in bed, plenty of fluid, and dietary measures are the important points in therapy. The principle of treatment rests on the fact that liver cells which can maintain ample stores of glycogen, protein, and vitamins, and have the normal amount of fat, have the greatest resistance to toxins and infection and are capable of the most regenerative power. The objective is to make the patient take as nutritious a diet as is possible, and it may be advantageous to keep the fat under 100 gm. per day. The duration and severity of the process determine the emphasis to be placed on the details of the diet and the need for supplementary measures. In the mild form of infective hepatitis known as catarrhal jaundice little need be done except to give fluids such as orange juice, lemonade, and glucose drinks, and a diet high in carbohydrate, low in fat, and to keep the patient in bed. The bowels may be kept open daily by a morning saline.

In more severe and more prolonged cases higher protein of good quality, as in meat and eggs, as well as increased carbohydrate, become of greater importance. The whole B complex vitamin, which plays an important part in the oxidation of carbohydrate, should be given by mouth (brewers' yeast, 25 to 75 gm. daily) or by hypodermic injection. In the severer forms of damage from unknown or violent toxins and infections the state of the patient prohibits sufficient intake, by mouth, of water (3,000 c.c. daily), essential protein, and carbohydrate. Under these circumstances intravenous infusions of glucose (5 to 10 per cent.) in quantities of 1 to 3 litres daily are important. Amino-acids (Amigen-Mead-Johnston) in 5 to 10 per cent. solution may also be given by this method, and a 50 per cent. glucose solution may be added to it. Protein hydrolysates can also be given by mouth, and are palatable. Depletion of serum protein can be improved by giving plasma or whole blood transfusions (250 to 500 c.c.) twice weekly. Methionine and choline are important substances for their lipotropic action, but their use in these cases is of uncertain value. Concentrated B-complex vitamin should be given hypodermically daily. If hæmorrhage occurs which is due to reduced prothrombin, vitamin K (2 to 4 mg.) every day or every second day may be tried, but is not as efficacious as in obstructive jaundice.

The rate of recovery varies, but patients should be kept in bed until normal appetite and a feeling of well-being return.

In those cases of toxic and infective hepatitis where recovery has been slow, prolonged adherence to diet, abstinence from alcohol, spices and condiments, and increased rest are advisable for months.

When severe necrosis (acute yellow atrophy) occurs little can be accomplished. Morphine should be given for relief.

Affections of the Blood Vessels of the Liver

By the layman, gastro-intestinal upsets of all types are apt to be ascribed to " chills on the liver." In actual fact there is little or no evidence that in such conditions the liver plays any appreciable part. The symptoms attributed to a disordered liver, such as anorexia, nausea, constipation, headache, or irritability, are probably more frequently due to a chronic gastritis or nervous dyspepsia.

In congestive cardiac failure, however, chronic venous congestion of the liver produces characteristic symptoms and signs which need further description.

Chronic Venous Congestion.—This results from the occurrence of congestive cardiac failure (*vide* p. 412). The liver is much enlarged, and on section shows a characteristic "nutmeg" appearance, due to the dark congested centres of the lobules, surrounded by paler areas of fatty degeneration.

Symptoms.—Rapid onset of hepatic congestion, causing increase in the size of the liver, produces epigastric pain and tenderness from sudden stretching of the capsule. When there is tricuspid incompetence the liver may be felt to pulsate, due to regurgitation into the hepatic veins. The impulse from the direct pulsation of the heart transmitted through the diaphragm must be distinguished from true expansile pulsation. This is best felt with one hand over the liver in the epigastrium and the other at the costal margin in the mid-axillary line. There is a feeling of fullness in the epigastrium, loss of appetite, often nausea and vomiting. There is an increase in the bile pigment in the blood plasma, the amount varying directly with the degree of heart failure, and there may be obvious icterus. Ascites is common, especially when there is œdema of the extremities.

Treatment is that detailed for cardiac failure (*vide* p. 415).

Thrombosis of the Portal Vein.—This rare condition is occasionally met with in cirrhosis of the liver. Malignant disease in the neighbourhood or in the liver may also cause thrombosis by infiltration of the vein wall and its lumen. Though not often diagnosed, it may be suspected where there is a sudden onset of severe portal obstruction with rapid increase in ascites and with hæmatemesis, melæna, and enlargement of the spleen, followed by severe symptoms of hepatic insufficiency.

Suppurative Diseases of the Liver

Suppurative Pylephlebitis.—This condition, often termed portal pyæmia, has become relatively uncommon since the importance of early operation in cases of appendicitis has been generally recognised. It may follow suppuration with septic phlebitis in any part of the area drained by the portal vein, most commonly the appendix and the rectum. The septic process spreads up the portal vein into the liver, and at autopsy there are multiple abscesses in the liver and sometimes pus in the portal vein.

The symptoms are those of a pyæmia with rigors; often, at first, few signs point to involvement of the liver, but in the later stages the patient generally becomes slightly jaundiced, and the liver is found to be enlarged and tender. The leucocyte count is high, and effusions, clear or purulent, may occur in the right pleural cavity.

The disease is usually fatal, but vigorous chemotherapy should be used.

Abscesses of the Liver.—Apart from portal pyæmia, amœbic abscess (*vide* p. 149), and actinomycosis of the liver (*vide* p. 72), hepatic abscess may result from suppuration of a hydatid cyst (*vide* p. 167). Suppurative cholangitis, usually secondary to obstruction of the common bile duct, may lead to multiple hepatic abscesses, and suppuration in the liver is a rare complication of trauma, such as bullet wounds, in this region.

Cirrhosis of the Liver

(Portal, Alcoholic, Laennec's Multilobular Cirrhosis)

Cirrhosis is chiefly a disease of males in adult life, but it is occasionally seen in women and children. Chronic alcoholism is by far the most important, though by no means its only cause, since in the great majority of heavy drinkers, cirrhosis does not develop. Also, cirrhosis does occur in total abstainers. The ætiology is not understood, but it is possible that it depends on a combination of factors which have to do with qualitative dietary insufficiencies with or without mild or repeated allergic or inflammatory liver reactions. Alcohol, in producing a chronic gastritis, would thus play a definite role in augmenting this process in a susceptible individual. Other substances such as spices, curries, and condiments may predispose to cirrhosis.

The disease at the present time is certainly less common both in England and in America than was the case thirty years ago. This decrease is the result of the greatly increased cost of alcohol and a resulting diminution in consumption.

Pathology.—The weight of the liver varies considerably (900 to 6,000 gm.), depending partly upon the relation between the compensatory hyperplasia, the degeneration of cells, the increase in fibrous tissue, and the amount of fat present. The term "atrophic cirrhosis" is applied when the liver is smaller than normal, but as far as the number of actively functioning liver cells is concerned, there is probably no great difference between the very large and the very small. Patients with cirrhosis who die of liver insufficiency usually have smaller livers than those who die from other causes. The surface is irregular, due to contraction of fibrous tissue and to proliferation of regenerating cells (hobnails). In the larger livers the surface may be merely coarsely granular; in the smaller the whole organ may be puckered and deformed; in both the capsule may be thickened and opaque from perihepatitis. On section, the hobnails have a yellow or tawny appearance, from which the name cirrhosis is derived. The liver substance is divided in a most irregular manner by greyish-white fibrous tissue which, spreading out from the portal areas, encloses a varying number of lobules (hence the term "multilobular"). The liver cells are compressed and degenerated. As a result of the portal obstruction produced by the fibrous tissue, collateral anastomoses for a compensatory circulation are extensive, and are carried out by the following sets of vessels:—

1. The gastric veins draining into the portal system anastomose with the œsophageal veins of the systemic circulation around the lower end of the œsophagus. With portal obstruction œsophageal varices may be formed, and, if ruptured, produce severe hæmatemesis.

2. The hæmorrhoidal (rectal) plexus forms an anastomosis between the superior hæmorrhoidal veins, which drain through the inferior mesenteric and splenic veins into the portal system, and the middle and inferior hæmorrhoidal veins, which drain into the inferior vena cava. Varices of the plexus produce hæmorrhoids, but the latter condition occurs so frequently in otherwise normal adults that their presence cannot be regarded as suggestive of cirrhosis.

3. The veins of Retzius connect the intestinal veins with the inferior vena cava and its retroperitoneal tributaries.

4. The para-umbilical vein running with the round ligament of the liver may form an anastomosis between the left branch of the portal vein and the veins of the abdominal wall. *Very* rarely this produces a bunch of prominent veins at the umbilicus known as a *Caput Medusæ*.

Symptoms.—As long as the collateral circulation and compensatory hyperplasia are sufficient there may be no symptoms. Thus there are latent cases in which discovery of the condition is due to accident or to the occurrence of some other disease. It is impossible to determine with any accuracy the length of time cirrhosis has been present.

The onset in cirrhosis is variable. Occasionally patients are encountered in whom a sudden, and often severe, hæmatemesis is the first sign. Less commonly there is a somewhat rapid onset of ascites due to portal obstruction. In most cases, however, there is a well-marked history of chronic dyspepsia which extends back for many years, and precedes any symptoms of cirrhosis. It must be clearly realised that the morning anorexia and vomiting, which are features of nearly all cases of cirrhosis, are due not to the liver condition but to a gastritis, usually induced by chronic alcoholism.

When the disease is fully developed the patient presents a characteristic picture. The nutrition is poor, with loss of subcutaneous fat, so that the face and neck are thin and drawn. The eyes are sunken, with an icteric tint. The complexion is of a dirty sallow hue. The skin is dry, inelastic, and may show pigmentation. The tongue is flabby and furred; the gums are spongy and bleed readily; the breath is offensive, and the lips dry and cracked. A ring of minute dilated venules in the lower thoracic region is often seen along the attachment of the diaphragm, but is, however, not uncommon apart from cirrhosis. The abdomen is enlarged by the ascites; the amount of ascitic fluid may be too great to allow satisfactory palpation, but with a lesser quantity the liver can often be felt by dipping down sharply on it. It is often considerably enlarged, diminishing in size as the disease progresses, though it may be small from the beginning. On withdrawal of fluid the sharp edge and the hard surface can be felt, and its granular or hobnail character can sometimes be made out. With marked atrophy, the area of liver dullness is decreased. The spleen is easily felt in many cases. Mild clubbing of the fingers, erythema of the skin along the sides of the palms of the hands and finger-tips, and telangiectases scattered sparsely over the body are common findings in patients with cirrhosis.

Slight jaundice is present in a third of the cases, but the van den Bergh test will show an increase in the plasma-bilirubin in a rather larger percentage. The reaction is direct, either delayed or biphasic. Slight irregular fever of 99° to 102° may be present.

In the earlier stages of cirrhosis the main symptoms are those of chronic gastritis. As portal obstruction develops, ascites becomes a prominent feature, and in addition there may be œdema of the feet. Hæmatemesis from rupture of œsophageal varices may occur, and is occasionally fatal. Later still, symptoms of hepatic insufficiency develop, and the patient may die of exhaustion and toxæmia.

Complications.—A very sudden onset of ascites usually indicates portal thrombosis, but it is a rare occurrence. Sometimes a chronic peritonitis aggravates the ascites due to portal obstruction. The fluid will then have a specific gravity of over 1·015, and polymorphonuclear cells are present. Patients with portal cirrhosis are very susceptible to intercurrent infection,

and may develop pulmonary tuberculosis and sometimes tuberculous peritonitis. Primary carcinoma of the liver is a rare complication.

Differential Diagnosis.—This is discussed on page 349.

Prognosis.—The prognosis depends mainly on the extent of the liver damage present when the patient is first seen. When this is considerable, whatever treatment be adopted, the outlook is poor. If the condition be discovered before the advent of ascites, and the patient live a strictly ordered life as to diet and rest, the disease may be arrested. Once ascites has occurred, little can be done; if, however, it be due to a complicating peritonitis, the fluid may disappear. Hæmatemesis, even though recurrent, is seldom fatal.

Once toxæmic symptoms appear, death will usually take place in a few months.

Treatment.—Many patients with cirrhosis are alcoholics, and complete and permanent abstention from all forms of alcohol should be insisted upon. Irritating substances such as spices, condiments, and highly tasting food should also be forbidden. The diet should be high in carbohydrates and protein and moderately low in fat. Brewers' yeast may be given, but there is probably no advantage in adding methionine and choline. Increased rest is important. The bowels may be kept regular by the frequent use of salines. In the ascitic stage tapping will relieve the abdominal discomfort (*vide* p. 366). Hæmatemesis should be treated by morphine, and blood transfusions may be necessary.

Hæmochromatosis (*Diabète Bronzé*)

This is a rare form of cirrhosis of the liver associated with some disturbance of iron metabolism, occurring chiefly in men of middle age. It is characterised by a remarkable darkening of the skin, which has a bluish-grey sheen due to the deposition of an iron-containing pigment, hæmosiderin. Weakness is the chief complaint, and there may be attacks of intestinal colic and great prostration. There is a hæmolytic anæmia of moderate degree, enlargement of the liver, and a palpable spleen. Hæmosiderin may be found in the urine. The deposition of pigment in the organs causes fibrosis. The pancreas is commonly affected, and often produces diabetes mellitus, which is difficult to control. This latter condition gives the disease its alternative name of bronzed diabetes. Hypogonadism, to a lesser or greater degree, results from deposition of the same pigment in the testes. There may be partial recovery, but usually death results from hepatic insufficiency and acidosis.

Hypertrophic Biliary Cirrhosis

The term "hypertrophic biliary cirrhosis" probably includes a number of different pathological conditions, all of which are rare. Hanôt in 1875 described a number of cases with enlargement of the liver and spleen with jaundice, abdominal pain, vomiting and fever, but it is doubtful whether the so-called Hanôt's cirrhosis is a clinical entity. It has already been mentioned (*vide* p. 339) that toxic or infective hepatitis may become chronic and lead to fibrosis and hypertrophy of the liver. Chronic infection or obstruction in the bile passages, such as may result from stones or infection

in the common bile duct, occasionally produces a secondary biliary cirrhosis.

The liver is usually very large. Its surface may be relatively smooth, or areas of regeneration may render it irregular. The spleen is also often enlarged and fibrotic.

Clinically there is a great variation in the symptoms of individual cases. Jaundice may be more or less persistent, or occur only in attacks, and gastro-intestinal symptoms, such as colicky pain, nausea, and vomiting, are not constantly present.

When hypertrophic cirrhosis appears to have arisen secondarily to chronic infection of the gall-bladder, cholecystectomy may prevent further damage to the liver. As the process now involves the liver cells, supportive treatment for them is the same as that given under the Treatment of Acute and Subacute Parenchymal Disease of the Liver (*vide* p. 343).

Syphilis of the Liver

In congenital syphilitic infants the liver and spleen are often enlarged, and contain great numbers of spirochætes. The liver cells are surrounded and compressed by a fine pericellular cirrhosis, and the infant usually dies at or shortly after birth. Congenital syphilis of the liver is also sometimes seen during adolescence. The condition then resembles the irregular gummatous liver of acquired syphilis.

In the secondary stage of acquired syphilis there may be an acute hepatitis, which results in jaundice, often associated with a painless but sometimes persistent hepatic enlargement. This must be distinguished from the jaundice which sometimes follows the administration of arsenical compounds, which is often homologous serum jaundice.

Tertiary Syphilis (*Syphilitic Cirrhosis of the Liver*).—Gummata are not very uncommon in the liver, and are much more frequent in men than in women, appearing ten to twenty years after infection.

Pathology.—Remarkable deformities result from the combination of scarring due to healed gummata and the nodules produced by more recent lesions. Multiple granulomatous areas with necrosis of the central portion are surrounded by a fibrous capsule, contraction of which, with absorption of the caseous centres, produces extensive puckering of the liver surface. Adhesions to neighbouring structures may develop. Amyloid degeneration may occur as a complication, and may involve also the spleen, kidneys, and intestine.

Symptoms and Signs.—There are often none, the gummata and cicatrices being discovered post-mortem. General symptoms of wasting, weakness, slight fever, and secondary anæmia without leucocytosis, occasionally precede abdominal discomfort or pain. With much fibrosis throughout the organ, or adhesions or enlarged glands in the portal fissure, there may be portal obstruction resulting in ascites; with gummata near the surface a perihepatitis or a syphilitic peritonitis may give rise to ascites. Chronic jaundice is rare, but may be associated with splenomegaly. Gummata of the liver often produce a most irregular enlargement of the organ, which may be easily palpable, and may be mistaken for a growth.

Differential Diagnosis is dealt with elsewhere (*vide* p. 349).

Treatment.—Large doses of potassium iodide (100 to 200 gr. daily)

should be given, together with bismuth (2 gr. bismuth salicylate) intramuscularly weekly for six to eight months with short interruptions after each ten injections. Penicillin in dosage of 400,000 units daily for two weeks should also be given. Arsenical preparations are to be avoided in these patients.

Malignant Disease of the Liver

Pathology.—Primary new growths in the liver, whether carcinoma or sarcoma, are very rare. The most frequent occurrence of primary carcinoma is in association with cirrhosis. In this form there are multiple small growths throughout the liver substance. The disease runs a rapid course, with signs of liver insufficiency.

The liver is more frequently involved by secondary deposits of carcinoma than any other organ. These produce some of the largest livers found at post-mortem, weighing up to 30 lbs. or even more. The primary growth is most commonly of the stomach, and next in order of frequency are the colon, œsophagus, pancreas, gall-bladder, uterus, and breast.

Symptoms and Signs.—Gradual enlargement with irregularity of surface is the chief characteristic of growth in the liver. Nodular masses with central depressions or umbilications can be felt or even seen through the abdominal wall. The organ may reach below the umbilicus. Sometimes the left lobe is more affected than the right, producing a large mass in the epigastric region. The deposits near the surface are apt to cause considerable pain and tenderness from perihepatitis, and friction rubs may be heard.

Jaundice is present in half the cases, but is seldom intense. Ascites occurs with about the same frequency as jaundice, but both in combination are less common. The ascites may be due to the pressure of nodules on the portal vein, but more often to extension of the growth to the peritoneum. The veins in the abdominal wall are enlarged, and rarely there may be nodules of carcinomatous tissue about the navel. The patient is markedly cachectic ; the face is cadaverous, and there is severe hypochromic anæmia ; weakness and loss of flesh are progressive. An irregular fever is frequently present, even without suppurative complications. Œdema of the feet is common. Widespread involvement of the liver ultimately produces death in coma from hepatic insufficiency.

Differential Diagnosis.—See below.

Treatment.—Morphine should be given freely when necessary, and the bowels can be kept regulated by salines and mild laxatives. When there is any possibility of doubt as to the diagnosis, an exploration is justifiable.

Differential Diagnosis of Hepatic Enlargement

Hepatic enlargement is often the most prominent feature in pathological conditions of the liver, but before considering the differential diagnosis it is important to stress the fact that not every palpable liver is enlarged. Weakness of the abdominal muscles and a general visceroptosis may result in the liver being considerably lower in the abdomen than is normally the case. In addition to such a ptosis of the organ, a thin abdominal wall facilitates palpation, and thus gives a false impression of the size of the liver. In such cases careful percussion of the upper border of the liver may show that the liver dullness does not extend up to its normal position in

the thorax, *i.e.*, the fifth intercostal space in the right nipple line. Too much stress, however, must not be laid on variations in the extent of the liver dullness, which is much influenced by such factors as emphysema or intestinal distension.

The causes of enlargement of the liver are tabulated below :—

1. Chronic venous congestion (nutmeg liver).
2. Abscesses (single or multiple).
3. The cirrhoses : (*a*) portal ; (*b*) gummatous ; (*c*) splenic anæmia ; (*d*) bronzed diabetes ; (*e*) biliary.
4. Growths, primary or secondary.
5. Cysts : hydatids.
6. Amyloid disease.
7. Hodgkin's disease and the leukæmias.

In the majority of cases a careful history and general physical examination are often sufficient to decide the diagnosis.

Acute infections of the liver resulting in abscess formation, whether single or multiple, are usually relatively easy to diagnose. Pyrexia of a hectic type, local tenderness over the liver, leucocytosis, and occasionally a rub, all suggest hepatic suppuration, which may be secondary to amœbic infections of the colon or to an inflammatory focus in the portal area.

The main diagnostic problems arise in the differentiation of hepatic enlargements due to growths, cirrhosis, and hydatid disease. Age and sex afford little help, and both with growth and cirrhosis emaciation and cachexia are severe. Chronic enlargement of the liver with little or no impairment of the general health is almost diagnostic of hydatid cyst. This diagnosis may be confirmed by an eosinophilia, a positive complement fixation test, or more rarely the finding of a hydatid thrill (*vide* p. 167).

In every case of hepatic enlargement, especially after the age of forty, careful search must be made for a primary growth which sometimes may give little evidence of its presence. Careful examination of the prostate, testicles, and breasts is important. Primary carcinoma of the liver is so rare that consideration of this possibility may for practical purposes be neglected. Secondary melanotic sarcoma may give rise to great hepatic enlargement months or even years after the primary growth in the eye or skin has been removed. Melanin is found in the urine. Of the cirrhoses, by far the most common is portal cirrhosis. A history of chronic alcoholism and evidence of chronic gastritis in the form of morning anorexia and vomiting will suggest this diagnosis. Newly formed spidery angiomata are also often seen in cirrhosis.

Pyrexia is common in the later stages of both growth and cirrhosis. Its presence, therefore, in a patient with enlargement of the liver does not exclude the possibility of these conditions.

If, in addition to hepatic enlargement, the spleen is also enlarged, the patient is probably suffering from cirrhosis rather than growth. If the splenic enlargement is considerable, and particularly if it is associated with secondary anæmia or hæmatemesis, Banti's disease is probable. Other types of cirrhosis such as Hanot's and bronzed diabetes are excessively rare. In the latter, pigmentation and glycosuria point to the correct diagnosis. In Hanot's cirrhosis the patient is much younger than is usually the case

in portal cirrhosis, and jaundice is a more marked feature. Ascites is common both with growth and cirrhosis, and has little diagnostic import.

Very valuable information is obtained from physical examination of the liver. With growth the organ is often very much enlarged and hard, but the most characteristic feature is the irregularity of the surface, which can be readily noted on palpation. The irregularities correspond to projecting nodules of new growth, which often attain a size of several inches in diameter. The umbilication of the deposits which is apparent at autopsy can sometimes be felt during life. In portal cirrhosis the liver surface feels hard, but it has not the gross bosses and irregularities palpable in growths. If the abdominal wall be very thin it may be possible to feel the roughening of the surface due to "hobnails." Extreme irregularity of surface is encountered in gummatous conditions of the liver; this is likely to be confused with secondary deposits, but a positive Wassermann test and a diminution in the size of the liver under treatment with iodides help to justify the diagnosis.

Abnormalities in the shape of the liver may lead to errors in diagnosis. A tongue-like projection of the right lobe of the liver may protrude downwards, and is known as Riedel's lobe.

A chronic solitary abscess may produce great enlargement of the liver, and is liable to be misdiagnosed as growth. Pyrexia, leucocytosis, and local tenderness may be completely absent. In doubtful cases laparotomy is advisable.

Amyloid disease of the liver may produce some of the largest livers encountered at autopsy. The organ is smooth, firm, and painless. The disease is usually generalised, and also affects the spleen, kidneys, and intestines. It occurs in suppuration of long standing, such as results from chronic osteomyelitis, empyema, and chronic tuberculosis. Anæmia, albuminuria, and diarrhœa are common.

DISEASES OF THE GALL-BLADDER AND BILE DUCTS

Cholecystitis

Acute Cholecystitis.—Acute cholecystitis occasionally occurs as a complication of enteric fever. Very rarely it may arise as a blood-borne infection. The inflammatory process often suggests an altered chemical state in the wall of the gall-bladder as a cause. Ascending infection from the duodenum is probably not an important factor. The *common* cause is the presence of gall-stones. Other predisposing causes are: (i) a previous inflammation; (ii) any condition favouring stasis in the gall-bladder. Commonly no organism can be demonstrated. Secondary infection with *Bacillus coli* frequently takes place. In cholecystitis associated with typhoid fever, the typhoid organism may persist in the bile for years.

Pathology.—In early lesions the mucosa is congested and œdematous. Later it becomes bright red or reddish-purple and covered with fibrinous exudate containing mucus. The wall is thickened, mostly from œdema. With more intense inflammation, such as occurs when a calculus is impacted in the cystic duct, suppuration may take place or necrosis of the wall result in perforation.

Symptoms and Signs.—Continuous pain in the right upper quadrant is the commonest symptom. It is sometimes referred around the costal margin or straight through to the right scapula. Deep breathing aggravates the pain. Usually vomiting and fever are present. The abdomen reveals tenderness under the right costal margin, rigidity of the right rectus, and lack of movement of the right diaphragm. An enlarged gall-bladder may sometimes be palpable, and may be felt quite low down in a few cases. Occasionally slight jaundice may be present due to extension of œdema into the common duct. A moderate leucocytosis is often present. Rigors are uncommon.

Acute Suppurative Cholecystitis. — If the condition progresses to suppuration, all the symptoms and signs, both local and general, become increased. Rigidity is greater, the fever and leucocytosis are higher, and the patient may be obviously toxæmic. Perforation results in a localised rather than generalised peritonitis and takes place without dramatic change in the symptoms and signs (see Complications of Gall-stones).

Diagnosis.—Differentiation from acute appendicitis may be difficult, especially when the appendix lies high in the abdomen. Acute pyelitis on the right side produces tenderness, more marked posteriorly than in front, and the urine will show pus. Biliary colic gives more agonising pain and no signs of local peritonitis, and this history may have preceded the present condition.

Treatment.—Many subside spontaneously, and conservative treatment with local heat and sedatives is advisable. Any increase in the signs and symptoms pointing to complications requires surgical intervention. The diet should be bland, in small amounts frequently. Chemotherapy is most disappointing in biliary infections. If much vomiting is present 5 per cent. glucose should be given intravenously. After the condition has completely subsided, cholecystectomy should be done.

Chronic Cholecystitis.—Chronic cholecystitis is usually the result of repeated acute attacks of biliary colic, with the presence of stones which obstruct the cystic duct repeatedly and cause prolonged inflammation. It may be associated with some degree of cholangitis. The gall-bladder, its wall thickened, may be shrunken and adherent to adjacent structures. The mucous membrane and muscle layer may be largely replaced by fibrous tissue, and there are areas of lymphocytic infiltration. The remnants of the mucous membrane become distorted and thrown up into adenoma-like masses. In addition, gall-stones are often present.

Symptoms and Signs.—These are mainly due to the prolonged inflammation subsequent to mild attacks of biliary colic. As these and mild attacks of acute cholecystitis are repeated, the inflammatory process overshadows the attacks of colic, and the disturbances of the motor function of the stomach and duodenum are characteristically variable and may resemble nervous dyspepsia and peptic ulcer. There is a feeling of fullness in the epigastrium with flatulence and nausea following meals, especially if condiments, food of high taste or roughness, or fried fat is taken. Pain is felt in the right upper quadrant and sometimes radiates through or around to the right scapula. Persistent tenderness in the right upper quadrant is usually present, and may be best elicited with the patient sitting up and the observer, from behind, palpates underneath both costal margins while the patient inspires deeply (Murphy's sign). Sometimes an indefinite mass may be

felt in the gall-bladder region, and this may include structures such as the omentum which has become involved and adherent to the gall-bladder. Test meals show no characteristic changes, but during or shortly after an exacerbation urobilin may be found in the urine and the stools may be pale.

Diagnosis.—Great caution should be exercised in the diagnosis of chronic cholecystitis. The larger proportion of patients with flatulence, upper abdominal pains, and chronic dyspepsia of various degrees are not suffering from gall-bladder disease, although cholecystograms may show a slowly emptying gall-bladder or even stones. Many are psychoneurotics, some have peptic ulcers, a few are due to food sensitivity, and still fewer are migrainous persons. A convincing history of repeated attacks of biliary colic and cholecystitis with tenderness limited to the gall-bladder region, present on many examinations, and X-ray studies which show intrinsic deformity or a failure to fill with dye with repeated tests are necessary for a correct appraisal of these patients.

Treatment.—Some improvement may be expected from medical treatment. This consists in a bland diet, frequent feedings, and small doses of phenobarbitone ($\frac{1}{4}$ gr.) or tinct. belladonnæ (15 minims) before meals. Those who do not receive benefit from a trial of this regimen should have surgical treatment, though the results are frequently disappointing, and careful medical treatment should be persevered with in order to secure normal motor function. There is no evidence that the avoidance of foods which contain cholesterol, such as eggs, kidney, liver, cream, and butter, is of any value.

Gall-stones (*Cholelithiasis*)

Ætiology.—Gall-stones may occur at any age, but the main incidence of symptoms is in women of forty or over who have borne children. The production of gall-stones is not yet understood, but probably depends on several factors. Infection is commonly the result, not the cause, of the precipitation of gall-stones. Stasis in the gall-bladder was also thought to be a cause, because pregnancy and obesity seem to be associated with the formation of gall-stones, but this explanation is not valid. As cholesterol is the commonest constituent of calculi, endogenous and exogenous sources of excessive amounts in the bile have been blamed, but without real proof, and in conditions where an increased blood cholesterol is common (*e.g.*, in some diabetics and myxœdema), gall-stones are not more frequent. It is possible that the relationship between the concentration of bile acid and cholesterol, together with the fatty acid concentration, the calcium content, and the *p*H of bile, are the more important factors in calculi production.

Composition of Gall-stones.—The commonest forms are those made up of cholesterol and bilirubin-calcium. They are usually multiple, dark brownish-green in colour, stratified, and often faceted, unless enormous numbers be present, when they are usually round. Single stones are pure cholesterol with or without a small outside layer of bilirubin-calcium. Pure pigment stones or mud occur in acholuric jaundice.

Symptoms and Signs.—There may be none. Ten per cent. of all autopsies reveal the presence of gall-stones, and the percentage is much higher in patients over seventy. The symptoms fall into three main types : (i) acute cholecystitis (*q.v.*) ; (ii) gall-bladder dyspepsia (*vide* Chronic Cholecystitis) ; (iii) biliary colic.

Biliary Colic.—Spasm of the smooth muscle in the wall of the cystic and common ducts, due to the presence or passage of calculi, causes intense pain. These attacks of colic may occur at any time; sometimes they follow exercise, or jolting, great indiscretion in diet, or may sometimes be brought on by intense emotional stress. The pain may be moderately severe or extraordinarily violent. The onset may be sudden, but usually begins with a pressing or bloated feeling rapidly increasing to agonising pain which may last from a few moments to many hours. The pain usually begins high in the epigastrium, but may be felt first in the right hypochondrium, where it commonly remains. It radiates around the lower part of the chest, or through to the back, to a position just medial to the inferior angle of the scapula. Occasionally it may radiate down the abdomen, up to the precordium or to the right shoulder. The pain is usually steady, but has waves of increased severity superimposed upon it. There is great restlessness, and the pain may be so extreme as to cause the patient to roll about. Vomiting, profuse sweating, and exhaustion can be severe. There is shivering without fever or leucocytosis. Sometimes the pain of biliary colic is less severe, and accompanying infection is the more prominent feature. There will then be fever which may reach 103°. In spite of great pain there is surprisingly little shock unless an acute pancreatitis complicates the picture. Following the attack considerable soreness is felt in the gall-bladder region, and there may be jaundice of varying degree and duration.

Effect of Calculus in the Cystic Duct.—Usually there is no visible jaundice, but if œdema or inflammation extends to the common duct there may be mild jaundice and bile in the urine, which is easily overlooked but helpful in diagnosis. Should the walls of the gall-bladder not be fibrosed, the organ may become greatly distended by mucus. After a time the bile pigment is absorbed, clear mucoid material remaining (mucocele). The enlarged gall-bladder forms a rounded tumour, palpable below the liver, sometimes extending below the umbilicus. It may be mistaken for a large kidney or an ovarian cyst. Under these conditions an acute cholecystitis may complicate the picture, and empyema of the gall-bladder is a common sequel. Ulceration of the wall and perforation may rarely occur.

Effect of Calculus in the Common Duct.—Single or multiple stones may be present. The usual site is the lower end, in the ampulla of Vater, where the diameter is least, but there may be stones throughout the common and hepatic ducts. The obstruction to the duct may be (*a*) complete, or (*b*) partial or intermittent.

(*a*) *Complete Obstruction.*—The ducts may become much dilated. The gall-bladder is usually not enlarged owing to a co-existent fibrosis due to cholecystitis. Jaundice is always present and is deep in hue. There is, as a rule, no fever.

(*b*) *Partial or Intermittent Obstruction.*—This is the usual effect of stones in the common duct. A calculus in the ampulla of Vater has a ball-valve action. The common duct may be so much dilated as to be almost cystic, and the dilatation continues into the hepatic and intra-hepatic ducts. The liver enlarges, but may decrease in size later, due to a secondary biliary cirrhosis (*vide* p. 350).

There is no enlargement of the gall-bladder, which is thickened by chronic inflammation. The type and radiation of pain is similar to that from cystic duct stones, but its position is possibly more commonly in the

epigastrium than in the right upper quadrant. Characteristic symptoms are attacks of chills and fever, nausea and vomiting, sometimes severe colic, marked jaundice, and lessened bile in the stools. These paroxysms (intermittent hepatic fever of Charcot) are due to infection of the ducts, and to some extent of the liver, when the obstruction becomes temporarily more complete. The chills are severe, and the fever may reach 105°. The van den Bergh test shows an immediate direct reaction, and there is a leucocytosis. These attacks may recur over a number of years. If suppuration take place in the ducts the fever becomes remittent; the jaundice is not so marked, but the liver increases in size and may be tender from suppuration. This is often a fatal complication.

Complications of Gall-stones.—Acute, subacute, and chronic cholecystitis are accompaniments of gall-stones, and can hardly be designated as true complications. A gall-stone in the ampulla of Vater may cause bile to flow up the duct of Wirsung (the pancreatic duct) and set up acute hæmorrhagic pancreatitis. But even in gall-bladder stone pancreatitis of varying degree is not uncommon. As a result of pericholecystitis, the gall-bladder may become adherent to neighbouring structures and inflammatory change spread to them with the possibility of the formation of abscesses or fistulæ. In the abdominal cavity fistulæ may form between the gall-bladder and any part of the gastro-intestinal canal. If a stone pass through a fistula into the lumen of the intestine it may be passed in the fæces, or, if large, it may produce acute obstruction (gall-stone ileus); this impaction most commonly occurs in the lower part of the ileum.

The Diagnosis and Differential Diagnosis of Biliary Colic.—The diagnosis is made by the typical position and character of the pain, and the presence of jaundice, or a history of its appearance in a former attack of pain. Biliary drainage soon after an attack will often show cholesterol crystals or calcium bilirubinate or both. Renal colic is usually felt first in the loin, or lower down in the abdomen, radiating to the bladder and genitalia, and the urine contains blood cells. The dyspepsia associated with gall-stones with cholecystitis may simulate that of duodenal ulcer very closely, and indeed, duodenal ulcer and gall-stones often coexist. A peptic ulcer on the posterior wall of the duodenum with perforation can be mistaken for biliary colic. It is rarely that œdema from a penetrating duodenal ulcer compresses the common bile duct to produce slight jaundice. Previous duodenal ulcer symptoms, greater tenderness not maximal under the right costal margin, and X-ray examination aid in differentiation, though adhesions of the gall-bladder to the duodenum may produce X-ray appearances somewhat suggestive of duodenal ulcer. The gastric crisis of tabes may imitate gall-stone colic, and the pupils and reflexes should be examined. Carcinoma of the common bile duct or head of the pancreas can be confusing alternatives in diagnosis, but jaundice is more continuous and there is less pain (see Diagnosis between Obstructive and Hepatic Jaundice, p. 342). Certain migrainous persons have severe abdominal pain due to pyloric or intestinal spasm which has been mistaken for gall-bladder disease, but a careful history should make it clear.

Treatment.—When the presence of gall-stones is certain, providing the clinical evidence is convincing that the symptoms and signs are in actual fact caused by them, cholecystectomy should be done. With palliative treatment further trouble is frequent, and operation may have to be undertaken

at a later date, possibly under less favourable circumstances and with much less probability of cure. Serious disease in other systems are obvious contraindications, and sedatives and anti-spasmodics such as small doses of phenobarbitone, atropine, and nitroglycerine, together with a bland diet, have to be tried. For biliary colic morphine with or without atropine is required, but nitroglycerine (gr. $\frac{1}{50}$) and the inhalation of amyl nitrite may be helpful in milder attacks.

Aids to the Diagnosis of Gall-bladder Disease

Radiograms of the gall-bladder region may show the shadow of stones, provided they are not pure cholesterol. A barium meal may show distortion around the pylorus or duodenum if there are adhesions from the gall-bladder.

Cholecystography.—The visualisation of the gall-bladder by dye substances such as phenol-tetra-iodophthalein depends on the fact that bile is concentrated in the gall-bladder by the absorption of water through the mucous membrane. The dye given by mouth is excreted by the liver in the bile, and if sufficiently concentrated in the gall-bladder render that organ opaque to X-rays. No concentration takes place in the bile ducts, so that shadows corresponding to them are not seen. *The use of the dye is contraindicated* in the presence of hepatic disease. This includes cases with marked jaundice. The dye can be given intravenously, but good results are obtained when the dye is given by mouth in the form of opacol, shadocol, or pheniodol. The drug dissolved in water is given at 7 P.M. with a meal consisting of carbohydrate but no fat. No more food is taken, and after fourteen hours using opacol or shadocol and sixteen hours using pheniodol, X-ray films are taken of the gall-bladder region. The patient then has a fatty meal, such as eggs and bacon, and two hours later a further X-ray film is taken. The normal gall-bladder is well visualised fourteen hours after the dye has been taken, but the later film taken after the fatty meal usually shows the shadow to be definitely smaller or even absent owing to the gall-bladder having emptied.

Alterations of the Gall-bladder Shadow in Disease.—(i) There may be no shadow; (ii) the shadow may be faint; (iii) filling defects may be present; (iv) the shape may be distorted; (v) the density may vary, or the time of appearance and disappearance of the shadow may be altered.

Interpretation.—The clinical interpretation of the significance of the X-ray findings is difficult and often misleading. The absorption of the dye from the intestine and its excretion by the liver is variable in different individuals and in the same person at different times. Obesity often interferes with the clarity of the films, and the amount of dye may be insufficient for the weight of the patient. Small solitary intestinal gas bubbles over the gall-bladder region may be confusing. The demonstration of stones is the most useful finding, but even a gall-bladder loaded with calculi does occasionally fill, look normal, and empty well. Also, a gall-bladder that fails to fill with dye, or fills poorly, or empties slowly, may be quite normal. Increased tone of the sphincter of Oddi or of the duodenum may delay the emptying of the gall-bladder. Repeated tests are therefore often necessary in order to establish a true diagnosis of malfunction.

PLATE 21

Non-opaque gall-stones, showing as filling defects in a cholecystogram. (From plate by O. A. Marxer.)

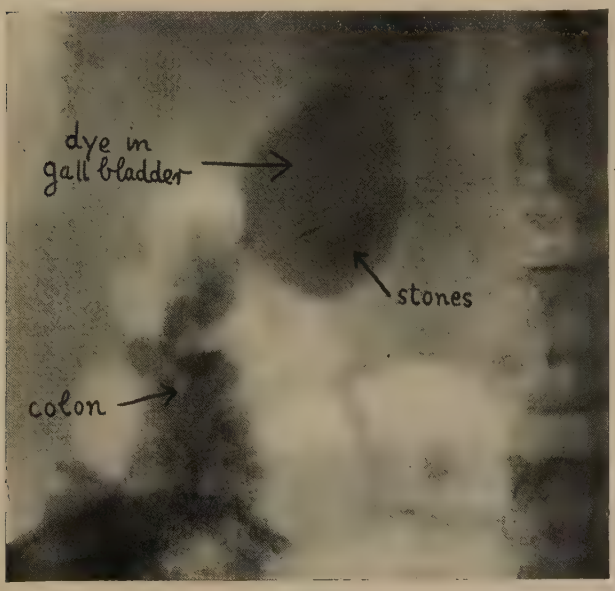

PLATE 22

Gall-bladder visualised by cholecystography, showing stones. Some of the dye is also visible in colon.
(From X-ray by Dr P. J. Briggs.)

[*To face page* 356.

Carcinoma of the Bile Passages

Ætiology.—Carcinoma may arise in any portion of the ducts or gall-bladder, but the gall-bladder is much the most common site. Its greater incidence in women is in keeping with their greater susceptibility to gall-stones. Gall-stones are a common antecedent, and are present in 70 to 90 per cent. of gall-bladder carcinomata.

Pathology.—The fundus of the gall-bladder is the usual site, but carcinoma may start anywhere, and if in proximity to the neck will obstruct the cystic duct. There may be a papillomatous outgrowth into the cavity of the bladder or a firm white infiltration of the wall. It is either columnar or spheroidal celled. Carcinoma of the bile ducts occurs most frequently in the lower end of the common bile duct or in the ampulla of Vater (ampulla of bile duct). The growth is columnar celled. Secondary growths may be found in the neighbouring lymph glands or liver.

Symptoms.—Where carcinoma follows cholelithiasis there are preceding symptoms of gall-stones or cholecystitis. The onset of malignancy may be accompanied by persistent pain in the right hypochondrium, with flatulence and loss of appetite. The patients lose weight rapidly. A hard irregular tumour often appears below the costal margin, directed towards the umbilicus, and may reach large proportions. It is usually mistaken for secondary carcinoma in the liver. Tenderness is only moderate, and rigidity of the right rectus not nearly as marked as in inflammatory conditions. The liver may become involved from direct extension or metastatic growths.

In *carcinoma of the common duct* or ampulla of Vater, there is a progressive obstructive jaundice (*vide* p. 338). Unlike carcinoma of the gall-bladder, it is more common in men. The stools are acholic ; the amount of pain is very variable ; colic occurs, but there may be no freedom from pain in the intervals. The gall-bladder becomes enlarged, and the liver is increased in size. The primary growth is not palpable, but some deep tenderness is present without marked rigidity. There is wasting and cachexia, and occasional slight fever. Ascites may ensue from peritonitis or pressure of enlarged glands in the portal fissure. Death results in a few months.

Diagnosis.—Carcinoma of the gall-bladder is recognised, when extensive, by the hard irregular tumour, with marked loss of weight occurring in an elderly patient with a history of gall-stones. In empyema of the gall-bladder, fever and leucocytosis are points of distinction.

The diagnosis of carcinoma of the common duct is more difficult. An important point of differentiation from gall-stone obstruction is the distension of the gall-bladder in the case of growth. Wasting and the absence of chills and fever are features of malignant stricture. Carcinoma of the head of the pancreas is often painless throughout the course of the illness.

Treatment.—Symptomatic treatment is all that is possible in carcinoma of the gall-bladder, operative procedures being out of the question by the time diagnosis is possible. In cancer of the common duct or ampulla, a cholecyst-duodenostomy may be done to relieve the obstructive jaundice.

DISEASES OF THE PANCREAS

Physiology.—The gland has two functions, the manufacture of insulin, which is produced by the cells of the islands of Langerhans, and the

production, by the cells of the acini, of the digestive ferments, lipase, trypsin, and diastase, which are excreted into the duodenum by way of the ducts of Wirsung (the pancreatic duct) and Santorini (the accessory pancreatic duct). The former joins the common bile duct to form the ampulla of Vater. The duct of Santorini is small and has a separate opening into the duodenum. The pancreatic secretion provides for the digestion of fats, proteins, and carbohydrates, and any diminution in the secretion is reflected in the character of the stools, though the disturbance must be considerable before this is evident.

Deficient pancreatic secretion renders the fæces bulky, pale, and oily, owing to an increase in their fat-content. This condition is described as steatorrhœa. The steatorrhœa that occurs in sprue, however, is not due to pancreatic insufficiency. If there be an interference with the passage of bile into the intestine, absorption of fats is still further hindered. The fat is present in the stools as soaps, neutral fats, and fatty acids, and there is also an increase in the number of undigested striated muscle fibres, a condition known as azotorrhœa. The fatty acids give the fæces a foul odour.

Diarrhœa is a constant accompaniment of achylia pancreatica, and may be very severe. There is no blood, but mucus may be present.

Laboratory methods for the detection of pancreatic insufficiency are not altogether satisfactory. Samples of the duodenal contents may be examined qualitatively for the presence of the pancreatic ferments, but quantitative estimations are difficult. The determination of the fat content of the fæces is also unsatisfactory. The most striking feature is the loss of nitrogen in the stools rising as high as 7 to 12 gm. instead of the normal of $1\frac{1}{2}$ to 3 gm. in twenty-four hours. The diastase index is sometimes used as a test of pancreatic efficiency, but its results cannot be regarded as conclusive. The test is based upon the fact that with obstruction of the pancreatic ducts diastase is absorbed into the blood and excreted in the urine. The latter normally contains 10 to 30 units of diastase, but with disease of the pancreas this figure may rise to 200 units.

Acute Hæmorrhagic Pancreatitis

Ætiology.—Previous or concomitant cholecystitis or gall-stones occurs in more than one-half the cases. The process, ill understood, involves some injury to the walls of the pancreatic ducts. This produces an activation of trypsinogen into trypsin resulting in self-digestion (necrosis) of the pancreas. Obstruction to the duct, the regurgitation of bile or intestinal juice, containing enterokinase, into the duct, infection from the duodenum, and acute vascular disturbances have all been suggested as possible causes, but without consistent evidence or proof. Trauma with hæmorrhage may be followed by acute pancreatitis.

Pathology.—The gland is swollen, reddened, and friable. Necrosis, gangrene, or suppuration may be seen in varying degrees; the activation of lipase produces fat necrosis, which is seen as opaque white areas in the neighbouring tissues, especially in the fat about the pancreas and in the omentum. The lesser peritoneal sac may contain sero-hæmorrhagic fluid.

Symptoms.—The typical attack is extremely severe. The onset is sudden, with intense pain in the epigastrium, often radiating to the left and going through to the back. It is usually a constant vice-like pain, but paroxysms

of increased severity may occur. Vomiting begins soon after the pain, and is persistent. The abdomen becomes distended and the condition may be mistaken for intestinal obstruction or acute peritonitis. The whole epigastrium is tender, but not markedly rigid. Deep palpation is possible, and occasionally a feeling of resistance is made out across the epigastrium, or the swollen head of the pancreas may rarely be felt. The patient is obviously very severely ill from the onset; the skin is moist and there is a mixture of pallor and cyanosis; the temperature is subnormal and the pulse rapid. Sudden loss of consciousness may even occur from shock. Glycosuria is uncommon. Death may occur in three or four days, but in less severe cases there will be gradual recovery in a week or two. Occasionally abscess formation takes place after a week or ten days, or a cyst containing sterile fluid may form. This may become infected after some weeks. Repeated attacks do occur.

Diagnosis.—An acute pancreatitis should be kept in mind in any instance of severe upper abdominal pain. It is difficult to distinguish from a perforation of a viscus or intestinal obstruction because of the persistent vomiting and general condition of shock. Points which suggest the condition are pain which is midline but radiates to the left or through to the left back, acute tenderness in the epigastrium with little or no rigidity. The patient is not restless and does not move about as in biliary or renal colic. If the condition occurs as a complication of cholecystitis it is suggested by the presence of pain and tenderness extending well to the left of the midline as well as that over the gall-bladder. If there is any fluid in the peritoneal cavity it will be stained with blood. In not a few cases the necrosis of the cells allows absorption of diastase (amylase) into the blood and excretion in the urine. The serum amylase may be found to be as high as 200 units (normal 10 to 30 units), but it fluctuates quickly so that a normal figure does not exclude severe pancreatitis.

Treatment.—The patient should be treated for shock and pain, and 5 per cent. glucose in saline given intravenously. Operation is to be avoided unless suppuration occurs, but in many cases a laparotomy is inevitable in view of doubts about the diagnosis.

Chronic Pancreatitis

Ætiology and Pathology.—Chronic fibrosis of the pancreas of a mild degree may be found during the course of routine post-mortem examination. Reports by surgeons that a chronic pancreatitis is present are often open to question, because palpation is difficult, and the size, shape, and consistency of the normal gland is subject to wide variations.

The commonest form of chronic pancreatitis is that characterised by an increase in the fibrous tissue between the lobules, and the gland is hard. The ætiology is obscure. Coexisting disease of the gall-bladder is frequent. Probably the most common cause is the repetition of mild attacks of acute pancreatitis that occur in association with acute cholecystitis with gall-stones. In spite of extreme fibrosis and atrophy of the gland, the islands of Langerhans remain unaffected. Another type of inflammatory change is an interacinar fibrosis with atrophy. This form is seen in a few cases of diabetes and in the rare disease hæmochromatosis, in which deposition of iron-containing pigment produces an interacinar fibrosis.

Symptoms.—It is difficult to recognise cases of interlobular pancreatitis, and many of those so diagnosed ultimately prove to be growths of the pancreas or disease of the biliary tract. It may be suspected in patients who give a history of recurring attacks of upper abdominal steady pain somewhat similar to biliary colic but reaching a peak of intensity after many hours and lasting several days and subsiding quite gradually. It is situated in the mid-epigastrium and in the left hypochondrium and from these through to the back. There may be a history of shorter attacks of mild acute pancreatitis at short or long intervals. During the attacks there may be vomiting, diarrhœa, mild fever; transient jaundice occurs from swelling of the head of the pancreas. A definite elevation of the serum amylase is suggestive, and steatorrhœa may be present. Glycosuria, recurrent during the attacks, may occur, and very rarely a temporary mild diabetic state may follow the attacks.

Treatment.—The ætiology being obscure, treatment is speculative. The gall-bladder, if it can be proved to be diseased, should be removed. Otherwise the diet should be low in fat and the barbiturates (phenobarbitone $\frac{1}{4}$ gr., nitroglycerine $\frac{1}{100}$ gr., or atropine $\frac{1}{150}$ gr.) before meals should be given a trial.

Carcinoma of the Pancreas

Pathology.—Carcinoma originates in the head of the pancreas in slightly over three-quarters of the cases. It is commoner in men than women. It begins either in the ducts or in the acini, forming a firm, hard mass, often infiltrating the gland. Owing to the localisation of the tumour in the head of the pancreas, glycosuria is uncommon. As the common bile duct is always more or less embedded in the head of the pancreas, it is usually obstructed as well as the pancreatic ducts.

Symptoms and Signs.—Steadily progressive painless jaundice is the most characteristic feature; anorexia, abdominal discomfort, nausea and vomiting, loss of weight, and fatigue are additional symptoms. In not a few cases, however, deeply seated epigastric pain, often extending through to the back, does occur. Itching of the skin is often intense, and the jaundice increases steadily to a deep olive-green. The liver is usually not enlarged, but the gall-bladder is distended, though not necessarily palpable. No pancreatic mass is palpable in two-thirds of the cases. The stools are continuously clay-coloured and fatty from the absence of bile, but there is no free fat. Loss of weight and strength is rapid, and cachexia soon follows. Should the growth arise in the body or tail of the pancreas, jaundice will not appear until later, and the first symptoms may be anorexia, loss of weight and strength, or deep-seated epigastric or back pain due to infiltration of the retroperitoneal tissues. Death usually takes place four to six months from the beginning of symptoms.

Diagnosis.—Progressive jaundice of obstructive type, usually without pain in a patient who is past middle age, is probably due to carcinoma of the pancreas or common bile duct. Other differential points are discussed under the Diagnosis between Obstructive and Hepatic Jaundice (*vide* p. 342).

Treatment.—The diet should be low in fats. The most distressing symptom is usually the intense itching, which may render life intolerable.

Ergotamine tartrate, 1 mg. hypodermically, may be used, and intravenous injections of 0·1 per cent. procaine should be tried ; 500 to 1,000 c.c. should be given very slowly. Fortunately, the obstruction can be relieved by cholecystgastrostomy, but operations to remove the growth are still in the experimental stage.

Pancreatic Cysts

Ætiology and Pathology.—The common types are pseudo-cysts formed by the collection of fluid in the lesser peritoneal sac following acute pancreatitis. Such cysts are often large ; they are not lined by epithelium, the walls being formed of connective tissue. True pancreatic cysts are rare and are either congenital retention cysts due to obstruction of a duct or cystic adenomata. These latter can also be big. The tail of the pancreas is the usual site. They are lined with epithelium derived from the pancreatic ducts or acini. In true cysts the fluid has a shimmering appearance, is reddish-brown in colour, and contains degenerated cells, traces of pancreatic diastase, and often cholesterol crystals. Multiple small cysts may occur in conjunction with congenital polycystic disease of other organs, such as the liver and kidney.

Symptoms and Signs.—The tumour due to the cyst is the most important sign. It is felt above the umbilicus in the midline or to the left under the costal margin extending to the midline. It may appear between the stomach and transverse colon, or between the lesser curvature of the stomach and the liver. The dullness on percussion may be continuous with that of the liver and spleen. The surface is smooth, with a rounded outline. If the tension of the contained fluid is not too great, fluctuation can be elicited. The mass may be the size of an orange, or may almost fill the abdominal cavity. It may or may not move on respiration.

Pain is a variable feature ; often there is none, but occasionally colicky pain is felt in the epigastrium, even before a tumour is palpable. There may be radiation of the pain to the left.

Nausea and vomiting may be troublesome and account to some extent for the loss of weight and weakness. Glycosuria may occur, especially when the tail of the pancreas is involved. Symptoms may result from pressure on the common bile duct, portal vein, or inferior vena cava. The enlargement is usually gradual, but hæmorrhage into the cyst may cause sudden increase in size with pain and slight fever.

Diagnosis.—The occurrence of sudden changes in the cyst, such as hæmorrhage, may lead to its discovery. In a pseudo-cyst there may be a history of an acute pancreatitis.

A radiographic examination with a barium meal or enema will demonstrate the relation of the cyst to the stomach and colon. Without operation it is impossible to diagnose the type of cyst. In the differential diagnosis a distended gall-bladder, mesenteric cyst, hydatid cyst of the liver, hydronephrosis, and ovarian cyst must be distinguished.

Treatment.—The cyst should be drained by operation. The patients usually do well, but recurrences are rather frequent. Occasional sequelæ to drainage are malignant degeneration in the wall of the cyst or the formation of calculi.

Pancreatic Calculi and Adenomata

Pancreatic stones are exceedingly rare and are seldom diagnosed during life. Chronic infection of the pancreatic ducts is the probable cause. They are soft, greyish-white in colour, and contain calcium. Owing to obstruction of the duct, they occasionally give rise to colic, which may be mistaken for biliary colic. They are very opaque to X-rays, but calcification, due to chronic pancreatitis within the pancreas, may be misleading.

Treatment is unsatisfactory.

Adenomata of the cells of the islets of Langerhans are rare. The tumour cells produce excessive quantities of insulin. The resulting clinical picture is one of chronic spontaneous hypoglycæmia (*vide* p. 240).

DISEASES OF THE PERITONEUM

Peritonitis

Inflammation of the peritoneum is caused by infection with micro-organisms, occurring either primarily or, more commonly, secondarily, following morbid processes in the contained viscera. The process may be generalised or local.

Ætiology.—*Primary Peritonitis.*—This somewhat rare form occurs as a terminal complication of gout, nephritis, and of any form of septicæmia. Also in this group are streptococcal and pneumococcal peritonitis, which, though usually blood borne, are often without any obvious focus of origin.

Secondary Peritonitis.—Inflammation of any of the organs within the abdominal cavity may lead to peritonitis ; this, however, is most commonly due to perforation of the appendix or of a peptic ulcer.

Bacteriology.—Peritonitis is usually a complication of pre-existing disease, and may result from any of the infections or other morbid conditions to which the abdominal and pelvic organs and the adjacent structures are subject. As might be expected, the bacteriology of peritonitis is very variable. The colon bacillus being a normal inhabitant of the gastro-intestinal canal, and having great facility for migrating through the injured wall, is, in consequence, frequently found in peritonitis. In the early stages it readily overgrows other organisms, and a pure culture is obtained. Later, however, it tends to die out. Various strains of streptococci are common. Infections with this organism occur sometimes in primary peritonitis and in that due to puerperal sepsis. The pneumococcus is found as part of a mixed infection, but also sometimes as a primary or hæmatogenous infection. The gonococcus is frequently the cause of a local peritonitis and, more rarely, of a generalised peritoneal infection.

Pathology.—In the earliest stage of a general peritonitis the peritoneal surface becomes dulled from congestion and œdema. A serous and fibrinous exudation takes place, and free fluid is found in the peritoneal cavity. The fibrinous exudate soon causes matting together of the organs, and the intestines ultimately become distended. The character of the exudate changes as the leucocytes increase until it may be thick and purulent. The particular organism predominating may determine the peculiarities of the exudation. In *Bacillus coli* infections the pus is thick, milky, and

foul-smelling. In virulent streptococcal peritonitis thin brownish fluid is found. In pneumococcal infection the pus is greenish and pseudo-membranous deposits may be seen.

In the healing process the exudate is either completely absorbed or there is organisation of the injured surfaces, so that firm fibrous adhesions are formed. The acute process may tend to become localised, especially when originating in the gall-bladder, appendix, or pelvic organs. Sudden perforation of a viscus spreads infection quickly over the whole peritoneal surface.

Acute Perforation of a Viscus.—The majority of cases of general peritonitis result from the perforation of a hollow viscus, and early diagnosis is of vital importance. The treatment consists in vigorous chemotherapy, the use of the Miller-Abbott tube, an adequate absorption of saline, glucose, and amino-acids intravenously, and, when biochemical disturbances have been corrected, surgical treatment.

Tuberculous Peritonitis.—*Vide* p. 104.

Pneumococcal Peritonitis.—This is more frequent in children than in adults, and is usually independent of, but may rarely be a complication of, pneumonia. The predominance of this form of peritonitis in girls suggests infection by way of the genital tract, and a pneumococcal vaginitis has been shown to be present in many instances. A bacteriæmia at the onset is demonstrable in half the cases. A pharyngitis may precede the peritoneal symptoms by two or three days. The onset is abrupt with high fever. Abdominal pain or vomiting may be the first symptom. The vomiting is persistent and may be projectile. Diarrhœa is constant at the onset, but later may be replaced by constipation. There is abdominal rigidity, general tenderness, and sometimes tympanites. The fever is high, but may show remissions. The leucocytosis exceeds 20,000 and often reaches 40,000.

The peritoneal exudate at first is thin and fibrinous and usually scanty, but becomes purulent and greenish in the later stages. It is most abundant in the pelvis.

The mortality among young children is very high, but between the ages of ten to fifteen recovery takes place in an increasing percentage.

In pneumococcal peritonitis it is doubtful whether surgical drainage of the peritoneum influences the course of the disease. It is, however, rarely possible to diagnose the condition with sufficient certainty to justify expectant treatment. Consequently, in the majority of cases operation is undertaken.

Streptococcal Peritonitis.—Apart from that occurring post-operatively and in the puerperium, this form is indistinguishable from primary pneumococcal peritonitis. However, the presence of a hæmolytic streptococcal pharyngitis sometimes gives the clue. In the puerperium the infection spreads by the lymphatics from a metritis, and the onset is sudden, the toxæmia profound, and the course rapid, with all the signs of a severe general peritonitis. Diarrhœa is commoner than constipation, and the vomiting may not be severe.

Gonococcal Peritonitis.—This form of peritonitis, much more common in females, is secondary to gonococcal salpingitis, or, in males, to epididymitis. The first signs are in the pelvis, but the infection may spread throughout the abdomen. The symptoms and signs are similar to other types of peritonitis. The prognosis as regards life is usually good, since the process

tends to become localised as a pelvic peritonitis. Troublesome adhesions may, however, result.

Chemotherapy is most successful in gonococcal infections, and usually in pneumococcal and streptococcal peritonitis, except where the organism has become resistant.

Local Peritonitis.—Inflammation in any of the abdominal viscera is accompanied by some degree of local peritonitis. The peritoneum in the liver region is involved in inflammation of the gall-bladder, in cancer, abscess, or hydatid disease of the liver, and in gastric and duodenal ulcers with subacute perforation.

Cholecystitis, appendicitis, and salpingitis are the most frequent causes of local peritonitis. The symptoms are localised in these areas, with rigidity of the muscle and tenderness maximal over the structure affected. Depending on the virulence of the infection and the occurrence of perforation, there is the possibility of spread of the peritonitis. The limitation of the infection by fibrinous adhesions results in the formation of a palpable mass. Suppuration may take place and subsequent rupture ensue in the absence of surgical drainage. If there be no suppuration the process will heal, leaving dense adhesions.

TREVOR OWEN.

SUBPHRENIC ABSCESS

Ætiology.—This condition is almost always secondary to disease in the abdomen ; very rarely it is a sequel to disease above the diaphragm. As would be expected, it more often follows disease of the upper abdominal viscera, the most frequent cause being perforation of a gastric or duodenal ulcer. The only common lower abdominal condition that may cause it is acute appendicitis. The spread of infection from the lower to the upper abdomen is by way of the paracolic gutters when the patient is lying on his back.

Morbid Anatomy.—It is usual to describe six separate positions in which a subphrenic abscess may form. Four of these are intraperitoneal, the coronary ligament being the chief dividing structure and giving right and left, anterior and posterior sites. The left posterior is an abscess of the lesser sac. The two extraperitoneal types of abscess are met with less often ; the right, which is the more common, lies in the region of the bare area of the liver and is usually the result of spread of infection from a retrocæcal appendicitis. The left may follow perforation of an ulcer or carcinoma of the stomach or colon into the retroperitoneal tissues ; it also follows pancreatitis. It presents in the left loin.

The extraperitoneal abscesses should be carefully distinguished from perinephric abscess, which has a different ætiology and a much better prognosis.

A subphrenic abscess is usually unilocular and single, although multiple abscesses may be met with. If secondary to biliary disease the pus in the abscess may be mixed with bile ; gas-forming organisms are often present.

Perforation through the diaphragm into the pleura or lung occurs in the later stages and, although sometimes affording temporary relief, is a serious sequel.

Signs and Symptoms.—The onset of a subphrenic abscess is often quite insidious, blending as it does with the course of the primary causal illness ; it is uncommon to find signs and symptoms pointing directly to its formation.

Owing to its serious nature and the importance of making an early diagnosis, the possibility of a subphrenic abscess should always be kept in mind.

Fever is always present and may be continuous with that due to the initial abdominal illness. At other times there is a period of normal temperature lasting perhaps as long as two or three weeks before pyrexia returns. In the early stages the fever is often continuous or remittent, later it assumes the swinging septic type. The patient wastes and looks pale and toxic. In neglected cases he becomes grossly cachectic.

When fever is noticed and search fails to reveal a collection of pus elsewhere in the peritoneum (*e.g.*, pelvis), infection of the subphrenic region should be thought of. The patient may complain of pain in one or other side of the chest; often he will admit to only a slight discomfort when questioned. Occasionally there is a severe pleuritic pain. The anterior intraperitoneal abscesses can present below the costal margin where they form a palpable tender mass. The posterior ones may give rise to tenderness over the lower ribs, and there may be actual œdema of the skin and subcutaneous tissues, though this is generally too slight to be detected by other means than pinching up a fold of skin and comparing it with the skin over the lower ribs of the opposite side.

Abnormal physical signs are often present at the base of the corresponding lung, either due to compression of the lung or to an actual pleural effusion. The classical picture of alternating zones of resonance and dullness, from above downwards, due to a layer of gas in the abscess below the diaphragm, may sometimes be demonstrated. These abnormal physical signs in the chest may lead to a diagnosis of pneumonia or empyema, while the underlying subphrenic abscess is overlooked. In subphrenic abscess without an accompanying pleural effusion the heart is not displaced as it is in the case of a pleural collection.

It cannot be too strongly stressed that if a patient has suffered from an intra-abdominal illness or operation and presents anomalous signs at the base of one lung, then a diagnosis of subphrenic abscess should be made and persisted in until every step has been taken to exclude it.

While the presence of a leucocytosis may confirm suspicion of the presence of pus, a figure below 10,000 per cubic millimetre is often seen in neglected cases, and therefore should not allay suspicions. The low figure is probably due to exhaustion of the bone marrow from severe toxic absorption. For the same reason a marked secondary anæmia is almost the rule in all but mild cases.

X-ray examination helps by showing a raised and immobile diaphragm, which may also be deformed; sometimes a subphrenic fluid level due to the presence of gas and pus is seen. In cases where doubt exists as to whether aspirated fluid is above or below the diaphragm, injection of some air, by giving a fluid level, will supply the answer.

In general, diagnostic needling to find a subphrenic collection is inadvisable, except as an immediate preliminary to operation, for infection of an uncontaminated pleura may readily follow. This pre-operative needling in any case in which the presence of a subphrenic abscess is suspected should be systematic and thorough and should include both subphrenic regions.

Prognosis.—Subphrenic abscess is always a serious condition; if not drained it carries a mortality of nearly 100 per cent. When drained the mortality is about 40 per cent. This is partly due to delay in diagnosis,

partly due to the fact that it so often complicates an already serious abdominal condition such as late perforation of a viscus or appendicitis with diffuse peritonitis. The infection also readily spreads through the diaphragm and adds a chest lesion to the patient's other burdens.

Treatment.—Drainage should be provided as soon as the diagnosis is confirmed. In many cases this involves rib resection, and especial care should then be taken to avoid infection of the pleura. This may make a two-stage operation necessary.

R. C. Brock.

ASCITES

Ætiology and Pathology.—The fluid may be a transudate or an exudate. The former occurs : (i) in myocardial failure ; (ii) in portal obstruction ; (iii) as part of a general dropsy in chronic nephritis ; (iv) rarely in chronic severe anæmia.

The degree of ascites in these conditions is always enhanced by a fall in the total serum protein below the critical level of 5 per cent., from whatever cause.

Ascites due to exudation is seen in various forms of peritonitis, such as those due to tuberculosis or carcinoma.

The Character of the Fluid.—The fluid in ascites due to transudation is clear and straw coloured with a specific gravity from 1010 to 1015, but not more. Its protein content is low, and it contains endothelial cells and a few lymphocytes. When due to exudation the fluid may be turbid and the specific gravity is over 1015. The protein content is much higher than that of a transudate, and the cells are lymphocytes in larger numbers, together with a varying number of polymorphonuclear leucocytes depending on the degree of the peritoneal irritation.

In malignant peritonitis tumour cells sometimes, and red blood cells frequently, are present. In syphilitic liver disease the Wassermann reaction may be positive in the ascitic fluid. In tuberculous peritonitis tubercle bacilli cannot be found, but inoculation of a guinea-pig results in the development of tuberculosis.

The quantity of fluid varies, ranging from a few hundred cubic centimetres to many gallons.

In *chylous ascites* the fluid contains fine fat globules but no leucocytes, and appears yellowish-white in colour. The specific gravity is usually above 1012. This condition is often associated with obstruction to the thoracic duct, which produces an escape of chyle from the lymphatics. A pseudo-chylous form also occurs in which the fluid contains only a small amount of fat in large globules and lecithin.

Symptoms.—The enlargement of the abdomen is the most noticeable symptom. The gradual distension finally produces pressure symptoms, consisting of gastric disturbances, dyspnœa from elevation of the diaphragm, and œdema of the feet and legs from compression of the inferior vena cava. The urine may show albumin and casts for the same reason. The flanks bulge in the recumbent position. The skin becomes tight and shiny. The costal margins are everted and the respiration is largely thoracic. The heart is displaced upwards. On palpation a fluid thrill can sometimes be made out by placing the palm of one hand on one side of the abdomen and flicking the opposite side with the finger. An enlarged liver or other tumour

can sometimes be felt by dipping down sharply through the fluid. On percussion there is a concave line of dullness curving around the sides and above the pubis. As the fluid increases the tympanitic central area becomes more and more limited until only the epigastric region under the xiphisternum remains tympanitic. The dullness will shift as the patient assumes different positions. When the ascites is considerable there is eversion of the umbilicus. Probably at least a litre of fluid must be present before it produces any signs.

Diagnosis.—The commonest cause of difficulty in the diagnosis of the presence of ascites is extreme adiposity of the abdominal wall. An apparent fluid thrill conveyed by abdominal fat may be mistaken for the true thrill due to fluid in the peritoneal cavity. In these cases the presence of movable dullness must be the sign relied upon. With the patient in the knee-elbow position, the most dependent part of the abdomen will be dull on percussion if there be any ascites.

Large ovarian and parovarian cysts may simulate ascites very closely. In these the dull area is central and the flanks are tympanitic. A distended bladder can be distinguished by catheterisation. Large hydatid and pancreatic cysts should not offer much difficulty. The sudden onset of ascites always suggests portal thrombosis.

Treatment.—Apart from the treatment of the cause of ascites, relief may be obtained by removing the fluid or retarding its formation. In hepatic cirrhosis, while the collateral circulation is being established, frequent tapping is necessary. Paracentesis may be done in the midline about half-way between the pubes and umbilicus or in the anterior axillary line.

The intake of fluid should be restricted to even as little as 800 to 1,000 c.c. In cases of myocardial failure, diuretics, in combination with digitalis, will often afford striking improvement. Saline purgatives should be given every morning. The amount of sodium chloride in the diet should be as low as possible. Mercurial diuretics such as mersalyl are often of great value (*vide* p. 418).

Carcinoma of the Peritoneum

Primary growths of the peritoneum are almost unknown, but secondary carcinomatous deposits are very common, especially as metastases from growths of the stomach or ovaries. They may vary in size from minute points little larger than a miliary tubercle to large masses of irregular shape. The omentum, mesentery, and pelvis are chiefly affected. Often owing to the associated ascites no tumours are palpable on abdominal examination, though rectal or vaginal examination may reveal hard nodules of growth in the pelvis.

The degree of ascites is variable. If fluid is withdrawn it may be clear or hæmorrhagic, and sometimes from obstruction and rupture of lacteals it is chylous. After tapping, masses of peritoneal growth may become palpable.

The condition has to be distinguished from tuberculous peritonitis and cirrhosis. In the former condition the patient is usually below the age at which cancer is common. Careful investigation of the history and physical examination may reveal evidence of a primary growth.

The prognosis is always bad, but sometimes in the case of ovarian tumours removal of the primary growth, together with deep X-ray therapy, may result in a striking improvement.

Trevor Owen.

DISEASES OF THE CARDIOVASCULAR SYSTEM

ANATOMY AND PHYSIOLOGY OF THE HEART

BEFORE considering the morbid changes that occur in the heart, a brief account is required of its normal physiological activities.

Close to the junction of right auricle (right atrium) and superior vena cava is to be found a small node of specialised neuromuscular tissue, about 2 cm. long, lying close beneath the endocardium. Developmentally it represents a remnant of the primitive cardiac tube, and is known as the *sino-auricular node* (sino-atrial node) of Keith and Flack (S-A node). A similar mass of tissue, the *auriculo-ventricular* (atrio-ventricular) node, lies beneath the endocardium of the right auricle about 1 cm. above the interventricular septum (ventricular septum). A prolongation of this tissue passes downwards in the interauricular septum (atrial septum) to the top of the interventricular septum, where it divides to form the left and right branches of the *bundle of His* or atrio-ventricular (A-V) bundle. These branches pursue a sub-endocardial course towards the apices of the ventricles, where they spread out to terminate in intimate connection with the musculature of the ventricular walls. This specialised tissue forms the only direct functional link between the muscle of the auricles and that of the ventricles, whereas part of the muscle of one auricle is continuous with that of the other, as is also the case in the ventricles.

Blood Supply of the Heart.—All three layers of the heart are richly supplied with blood vessels. The main ventricular supply is through the right and left coronary arteries, which arise just above the anterior and left posterior aortic cusps respectively. They break up into a fine network of smaller vessels and ramify throughout the organ. The left coronary artery supplies the bulk of the left ventricle, the interventricular septum, a portion of the anterior surface of the right ventricle, and the left auricle. The right coronary artery supplies the right auricle, the right ventricle, and a small part of the left ventricle.

During systole, owing to compression by the contracting muscle, the coronary flow ceases, and is resumed during diastole. Blood also reaches the intermuscular spaces from the ventricular cavity by way of channels known as the intertrabecular spaces or veins of Thebesius. In man their share in maintaining the circulation of the organ is probably greater than has hitherto been imagined. Anastomoses between the branches of the coronary arteries are limited, an anatomical consideration that emphasises the gravity of coronary occlusion.

Nerve Supply.—A large number of fibres from the right vagus proceed directly to the sino-auricular node. The cardiac fibres of the left vagus end near the auriculo-ventricular node and the A-V bundle, in which also nervous tissues are abundant. Fibres from the sympathetic system are distributed throughout the organ, the coronary vessels, and the aorta.

Mechanism of the Heart Beat

Heart muscle is so constituted that any excitatory stimulus causing contraction of one fibre will be conducted to all other fibres with which it is connected by muscle tissue. Since cardiac muscle fibres are intimately connected so as to form a syncytium, it follows that an effective stimulus applied to one auricle will cause a wave of contraction to pass over all regions of both auricles. The same is true of the ventricles. Heart muscle invariably obeys the "all or none law," in that once excited it contracts to its fullest extent. It possesses a particularly long refractory period, so that anything in the nature of a tetanic contraction is impossible, individual contractions being separated by appreciable intervals.

The sino-auricular node has been termed by Lewis the "pacemaker" of the heart and is a centre for the rhythmic production of a stimulus capable of exciting the surrounding auricle to contract. As the contraction begins at the S-A node, which lies near the openings of the great veins, the closure of these is brought about by the shortening of the fibres encircling the orifices. The blood in the auricles is thus forced towards the still quiescent ventricles. When the wave of contraction reaches the A-V node, the excitatory process is picked up by this tissue and passed on to the ventricular muscle by way of the A-V bundle and its ramifications. Since the speed with which this junctional tissue conducts the impulse is relatively high, the ventricular tissues contract very nearly simultaneously, the mitral and tricuspid valves close, and the blood is forced in the direction of the aortic and pulmonary vessels. The mitral and tricuspid cusps are prevented from being forced through the auriculo-ventricular orifices by the action of the chordæ tendineæ. When the ventricles relax, the aortic and pulmonary cusps snap together, while the mitral and tricuspid valves open to admit auricular blood.

The time occupied by one complete beat followed by the period of rest is termed the cardiac cycle. Clinically, this is defined as the time between the beginnings of the first sounds in two successive normal beats. When cardiac muscle contracts it is said to be in systole, and when resting and relaxed, in diastole. The cardiac cycle is in turn subdivided into systole and diastole. The former extends from the beginning of the first sound to the beginning of the second, and the latter from the beginning of the second sound to the next first sound. The heart of an adult beats normally between 60 and 80 times per minute, and at this rate the cardiac cycle occupies about $\frac{8}{10}$ sec. Ventricular systole lasts about $\frac{3}{10}$ sec. and diastole about $\frac{5}{10}$ sec. when the rate is 72. The velocity of the pulse-wave from the aorta to the wrist is such that the radial pulse becomes palpable nearly $\frac{1}{5}$ sec. after the apex beat is felt. This fact is of importance when timing abnormal sounds or thrills, for conclusions as to whether a murmur is systolic or diastolic may be quite misleading when the radial pulse is used as a measure of systole. In timing murmurs systole is best gauged by palpation of the apex beat or the carotid pulse. It must be realised, however, that with a rapid heart action the character and pitch of an apical murmur provide the chief means whereby it can be defined as systolic or diastolic.

Cardiac Efficiency.—A healthy heart has an ample reserve of power for the maintenance of the circulation under all conditions of strenuous exertion. There is no evidence that a healthy myocardium can be damaged permanently

by strenuous physical exercise. Before this can occur, fatigue of nervous or skeletal tissues enforce the cessation of effort.

In the past, undue stress was laid upon the presence of physical signs, particularly murmurs, in the estimation of the severity of cardiac conditions, but to-day the reaction of the heart to exercise is regarded as the factor of prime importance. Many tests of cardiac efficiency are advocated. Though differing in detail, they are all based on the fact that in health the heart rate is accelerated by exercise and rapidly returns to normal after the cessation of effort. The pulse is taken for 15 sec. with the patient standing. He then places one foot on a chair, the other being on the floor, and raises himself till both feet are on the chair, then lowers himself till one foot is on the floor. This is repeated twenty times in 60 sec. At the end of the exercise the pulse is taken for 15 sec. He then stands still for 45 sec. and the pulse is then taken again for 15 sec. This pulse reading should not be appreciably higher than the original resting rate. If during the exercise or immediately following it there are signs of undue dyspnœa and distress, cardiac efficiency is obviously impaired. Not uncommonly a patient's own story may be of as much or more value than an exercise tolerance test. Thus a walk from the station that formerly was not noticed may now produce breathlessness or a sense of distress.

It must be realised that exercise tolerance tests may be unsatisfactory as a result of non-cardiac conditions, such as emphysema, anæmia, and low grade infections, and even in the case of healthy hearts, give results dependent on the training of the individual. Thus the trained athlete may be able to perform with ease an exercise which would overtax the capacity of an untrained man.

In healthy persons excessive exertion results in a marked increase in pulse-rate, and in rate and depth of respiration. In addition, there may be sweating and subjective symptoms of distress, such as palpitation and even precordial discomfort. This combination is known as *the physiological syndrome of effort*, and occurs in all individuals after what to them represents excessive exercise. Exertion which produces violent palpitation in an undersized clerk would hardly change the pulse-rate of a blacksmith. Hence in judging the exercise tolerance of an individual it is important to take into account his life and habits.

PHYSICAL SIGNS OF THE NORMAL HEART

The physical signs of the heart vary with change of posture, and it is a good rule, whenever possible, to examine patients standing up, lying down, and *lying on the left side*. Exercise and respiration also influence the character of the cardiac sounds. The following is a brief summary of the findings based on the examination of a large number of normal hearts.

Inspection.—On inspection, there is symmetry of the left and right halves of the thorax, and no precordial bulging. A maximal cardiac impulse, corresponding with the apex of the left ventricle and the left border of the heart, may be observed in adults usually in the fifth but sometimes in the sixth left interspace from 7·5 to 11·5 cm. (3 to 4½ in.) from the mid-sternal line, according to the build of the individual. The visible impulse may be limited to an area of the size of a shilling, or it may be diffused over a large area and even reach the epigastrium. Frequently it is completely absent. *The apex*

impulse is the most reliable physical sign we possess of the position of the left border of the heart. Its position should always be described by stating the distance between the outer limit of the maximal impulse and the midline, as well as the intercostal space in which it is palpable. Statements regarding the position of the apex beat in relation to the nipple are misleading, but its relation to the mid-clavicular line helps to relate the actual measurement to the build of the patient. Visible pulsation may also occur normally at the second right and third left interspaces. The position of the apex impulse varies with posture, and when the patient lies on his left side it moves towards the axilla for a distance of about an inch. The veins of the neck are hardly visible in the upright position, but may bulge and pulsate visibly when the subject is supine.

Palpation.—When the impulse is diffuse, the region of maximum thrust may be taken as the apex beat. Sometimes when there is a diffuse impulse. and particularly during rapid heart action, there may be a sensation of a coarse vibration over the entire precordium during systole.

In children the apex beat may be higher than in adults, and is sometimes found in the fourth space.

Percussion.—Percussion should not be used in determining the position of the left border of the heart. This organ is overlapped by the left lung to a variable extent, which seriously interferes with percussion, especially in patients of middle age and over. If the apex beat is not visible or palpable, the size of the heart can only be defined with certainty by means of an X-ray examination. Normally, there is no impairment of note to the right of the sternum ; if there is, the impairment is due to the right auricle. Anatomically, the right border of the heart is mainly right and left auricle, and the left border mainly left ventricle, whereas almost the entire portion of the heart covered by the precordium is right ventricle, which is partly covered by lung to a depth that varies with respiration.

The Heart Sounds. — To simplify classification of heart sounds the precordium is divided into four areas : the *aortic area* at the second intercostal space to the right of the sternum ; the *pulmonary area* at the third interspace on the left border of the sternum ; the *mitral area* roughly corresponding with the region of the apex beat and a little internal to it ; and the *tricuspid area* at the sixth right costosternal junction and lower end of the sternum. Over these areas are best heard the normal sounds originating at the corresponding valvular orifices.

In the majority of normal subjects the only sounds heard over the precordium are the first and second heart sounds. In a fair percentage of persons, however, in whom there is no discoverable disease of heart or lungs, other sounds may be occasionally heard. Among these are blowing sounds or murmurs varying in intensity, heard best at one or other area and *always* systolic in time. They may vary with posture and the respiratory movements. or disappear and reappear for no obvious cause. They are often described as *cardiorespiratory murmurs.* The first or second sound may be reduplicated. Whenever such additional sounds are heard, they should suggest a specially careful examination of the cardiovascular system for evidence of disease, but should not in themselves be taken to indicate a structural change.

If the stethoscope is placed over a large superficial artery, nothing is heard unless the vessel is compressed, when an intermittent blowing sound simultaneous with the pulse is audible. Such a murmur is sometimes

encountered during auscultation below the outer end of the clavicles and is obviously of no pathological significance.

Normal Sensations referred to the Precordium.—The majority of persons are not conscious of their heart beat, except sometimes after exercise, when the physiological response to effort is present. Those of a highly excitable temperament or emotional instability may be abnormally conscious of their thoracic and abdominal viscera, the heart particularly, although a careful examination reveals no evidence of organic disease. In such subjects rapid heart action and palpitations are to be regarded as of nervous origin and not as signs of a diseased heart.

PHYSICAL SIGNS SUGGESTING CARDIAC DISEASE

Unfortunately, specific structural changes do not always lead to specific physical signs that would render diagnosis a straightforward and simple matter; indeed, conspicuous anatomical changes may occur without giving rise to specific physical signs, and be discovered only at autopsy. In general, however, it may be said that the presence of certain well-recognised physical signs is not only pathognomonic of cardiac damage, but signals damage of a particular character. The most important of these is cardiac enlargement.

Enlargement of the Heart.—The most certain indication of organic heart disease is cardiac enlargement. This is true whether the increase in size is due to hypertrophy or dilatation. Cardiac enlargement known to have been of rapid onset and short duration suggests dilatation, perhaps complicated by a pericardial effusion. Persistent enlargement present for several months suggests that hypertrophy is almost certainly a factor. In a heart known to have been enlarged for many months but more or less stationary in size, it is not possible to assess how much of the enlargement is due to hypertrophy and how much to dilatation. Nor is it of prognostic import to differentiate between them. All that is necessary is to remember that *while all diseased hearts are not enlarged, yet all unquestionably enlarged hearts are diseased.* So dogmatic a statement as this raises the question whether there is, in the case of the heart, no such process as a purely physiological hypertrophy in response to increased work over a considerable period, such, for example, as occurs without any evidence of disease in one kidney after the other is removed. From available data the conclusion seems inevitable that enlargement that can be detected clinically should never be regarded as of a physiological origin. Healthy men who have lived physically strenuous lives, such as athletes and manual labourers, do not show clinical cardiac enlargement in the absence of coincident disorder referable to the cardiovascular or renal systems. Insurance statistics also show that the expectation of life is diminished in persons with enlarged hearts and no other signs or symptoms of disease.

We may thus conclude that chronic enlargement is the result of chronic disease, whether progressive or arrested; and that acute enlargement heralds an acute condition, whether due to anæmia or inflammation of the myocardium.

It is important that a heart displaced by scoliosis or pulmonary disease should not be mistaken for one that is enlarged.

Precordial Thrills and Cardiac Murmurs.—By a thrill is meant a vibration of the thoracic wall felt over the cardiac area and communicated to the hand

during palpation. It is always accompanied by a murmur, though the converse is not true. Murmurs (*bruits*) may be high pitched and blowing or low pitched and rumbling, and sometimes may have a musical quality. They occur at any period of the cardiac cycle. They may precede, lead up to, or follow the usual heart sounds, or replace one or other of these entirely. They may be loud and readily audible, distant and faint, or vary in intensity.

The significance of a cardiac murmur is often a difficult problem. As a general principle it may be said that all diastolic murmurs indicate organic disease. Systolic murmurs on the contrary do not necessarily imply any pathological condition. To reach a decision as to the significance of a systolic murmur it is necessary to take into account many factors, such as the age of the patient, the likelihood of congenital heart disease, his record as regards previous diseases, particularly rheumatic fever, chorea, and syphilis, and any other abnormal physical signs found in the examination of the heart. Provided the patient is under middle age, has no history of rheumatic fever, chorea, or syphilis, has a good exercise tolerance and displays no other physical signs of cardiovascular disease, it is unlikely that a systolic murmur, whatever its site or distribution, is of pathological significance. It is not uncommon to find at autopsy no structural abnormality of the heart or great vessels when during life a loud systolic murmur had been present.

Systolic murmurs may alter in character or intensity with change in posture and with different phases of respiration. Such murmurs are often termed cardiorespiratory and are of no pathological significance. Sometimes in diseases affecting the lung, such as pneumonia, abnormal sounds synchronous with cardiac systole may be heard. These are described as exocardial murmurs or sometimes as pleuro-pericardial friction sounds. They have no special significance.

Apart from the systolic murmurs so often heard in apparently normal hearts, particularly when the pulse rate is high, they are heard also in the following conditions :—

1. Cardiac enlargement, acute or chronic.
2. Valvular disease, acquired or congenital, and patent ductus arteriosus.
3. Dilatation of the aorta or aneurysm.
4. Atheromatous changes in the valves.
5. Hyperthyroidism.
6. Anæmia.
7. Convalescence from acute infections.

A systolic murmur developing in the course of rheumatic fever may be the first sign of a mitral endocarditis. Where there is underlying structural alteration in the heart or great vessels, systolic murmurs are usually uninfluenced by posture and the respiratory phase. The association of a thrill with a murmur is indicative of organic change.

It is important to realise that auscultatory findings form only part of the evidence on which a particular diagnosis is based. The entire clinical picture is the only safe basis on which to found the final conclusion, ætiology being always of extreme importance. The types of murmur associated with lesions of the different valves are discussed in the section dealing with chronic valvular disease (*vide* p. 396).

DISTURBANCES OF RATE AND RHYTHM

When the heart is beating normally, the stimulus initiating contraction arises in the S-A node. A contraction may, however, follow a stimulus originating elsewhere in the myocardium, and such a beat is often spoken of as *ectopic* in origin.

The rate of origin of normal stimuli arising in the S-A node is under the influence of the vagus nerve, vagal stimulation leading to slowing. Stimulation of the sympathetic accelerates the heart rate, but its action is incompletely understood. Ectopic foci may exist anywhere in the heart muscle, and give rise to isolated beats, or to a series of regular beats for varying periods of time. Particularly is this the case when there is active disease. The passage of an excitatory impulse, wherever it may arise, may be interrupted in its course by so-called "block" in the junctional tissues, or by meeting a portion of muscle still in the refractory state. These simple principles form the basis of our knowledge of irregularities of the heart beat.

The Electrocardiograph.—This instrument is in extensive use; it seldom affords much information of value in valvular disease, but is decisive in the elucidation of obscure arrhythmias. In suspected myocardial disease in elderly patients and in all cases of thoracic pain the electrocardiographic findings are important. A brief description of electrocardiographic findings will be appended in the following sections. A normal electrocardiogram is shown in Fig. 11.

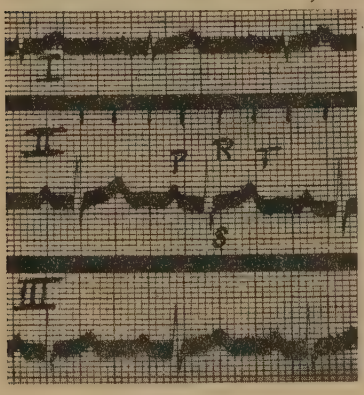

FIG. 11

Electrocardiogram from a normal subject, showing the three standard leads. The time marker in this and subsequent figures shows fifths and twenty-fifths of a second.
(*From E.C.G., by Dr Maurice Campbell.*)

The small deflexion P is associated with the excitation of the auricles, and the deflections Q, R, S, and T with excitation of the ventricles. The interval between the beginning of P and the summit of R is regarded as the time taken for the wave excitation to travel from the S-A node to the ventricular muscle. This P-R interval is related to the conducting capacity of the junctional tissues, and in the normal heart does not exceed 0·2 sec. Electrocardiography has grown to be almost a separate branch of the study of heart disease, and an enormous literature has accumulated. For ordinary clinical work, Einthoven adopted the leads: Right Arm—Left Arm=lead I; Right Arm—Left Leg=lead II; Left Arm—Left Leg=lead III. These leads are now in general use.

An effort has been made to explore the electrical field round the heart by contacts placed close to this organ, and a lead, so-called lead IV, has been used. In this one contact is placed on the chest wall just outside the position of the apex beat and the other is on the right arm (lead IV R) or left leg (lead IV F), usually the latter. This lead has been standardised, and is certainly of value in research and sometimes provides conclusive evidence of coronary infarction or pulmonary embolism where the other leads fail to do so; it is still uncertain if this happens

frequently enough to justify the extra complications of its routine use for clinical purposes.

Tachycardia and Bradycardia

By tachycardia is meant a conspicuous increase in the heart rate with or without disturbance of rhythm. It may continue for long periods or may be limited in duration to a few hours or even a few seconds.

A simple tachycardia is present when the stimulus production in the S-A node is increased in frequency above the normal rate for the individual in question, and when it is not characterised by an abrupt onset and an equally abrupt cessation. The latter characteristics define a special form of irregularity of rhythm to be described later, namely, *paroxysmal* tachycardia. Simple tachycardia is the physiological response to exercise, excitement, fear, and emotion. It also commonly accompanies any of the following conditions: (i) Pyrexia, when the pulse-rate increases roughly by 10 for every 1° F. rise in temperature; (ii) convalescence from debilitating disorders; (iii) anæmia; (iv) disease of the heart muscle; (v) hyperthyroidism; (vi) hysteria, the menopause; (vii) pregnancy; (viii) intoxication with drugs such as alcohol, tobacco, atropine, and thyroid extract.

Simple tachycardia is a symptom of some underlying condition, and disappears when this is removed. It seldom exceeds 130 beats a minute for long; when it does so, the heart's action may become seriously embarrassed and this leads to distressing symptoms. In simple tachycardia the pulse-rate is influenced by changes in posture; it is also increased by the action of atropine on the vagal nerve endings. On the other hand, in paroxysmal tachycardia, or that due to flutter of the auricles, variations in posture and administration of atropine are without effect on the pulse-rate. In the condition known as the "effort syndrome" (*vide* p. 425), the tachycardia is simple in type, but may be complicated by extrasystoles. In early phthisis tachycardia may be one of the earliest physical signs. In acute and subacute rheumatic infections persistent tachycardia may be the only sign of a serious cardiac involvement, necessitating prolonged rest in bed until the pulse-rate has returned to normal.

In simple tachycardia the electrocardiograph reveals normal auricular and ventricular complexes with, if anything, a shortening of the P-R interval.

Bradycardia.—Heart rates below 70 are common both in health and disease. A heart rate of 40 or below is, however, suggestive of heart block (*vide* p. 380). Rates between 40 and 60 are often encountered during convalescence from acute illness, during and after jaundice, in conditions involving cerebral compression, and in 2 to 1 heart block. An abnormally slow heart rate, *e.g.*, 40 to 50, is sometimes found in healthy athletes.

Abnormally low pulse-rates due to non-transmission of the ventricular beat to the wrist, as in digitalis poisoning with pulsus bigeminus (*vide* p. 386), do not constitute true bradycardia.

Sinus Arrhythmia

The heart rate accelerates during inspiration and slows during expiration. This arrhythmia is most obvious in children and young adults, in whom it is described as sinus arrhythmia. It is due to changes in the rate of origin of impulses in the S-A node and is of no pathological significance. In an

emotional tachycardia the detection of sinus arrhythmia is of value in supporting the diagnosis.

Other Sinus Irregularities.—In some people the heart rate varies under vagal influence without relation to the respiratory movements. A common example of this condition is the ordinary fainting attack in apparently healthy individuals, when the heart rate may drop to 50 and is accompanied by a sudden fall in blood pressure. The condition is specially common in persons showing the "effort syndrome." Sometimes the feeling of sudden faintness may develop into actual loss of consciousness. All sinus irregularities disappear under the influence of atropine, exercise, amyl nitrite, and fever.

Extrasystoles

When the heart contracts following an impulse arising outside the S-A node, the contraction is described as an extrasystole or premature beat. Such beats may originate in the muscle of either auricles or ventricles and are described as auricular or ventricular extrasystoles. Nodal extrasystoles arise near the A-V node. They may occur singly and at long intervals, scattered frequently throughout an otherwise regular rhythm in runs of twos and threes, or, as in paroxysmal tachycardia, in a continuous stream persisting for a considerable period. Nodal and ventricular extrasystoles are followed by a compensatory pause, as the ventricle is refractory to the next impulse transmitted from the auricle. With an auricular extrasystole this pause does not occur, as the following impulse from the S-A node is sufficiently delayed to allow the ventricle to pass out of its refractory period. Examples of extrasystoles are shown in Figs. 12, 13, 14, and 15. When extrasystoles alternate with normal beats they give rise to the so-called pulsus bigeminus, a rhythm characteristic of digitalis poisoning.

Extrasystoles occur at all ages and under all conditions, but their incidence is greatest after fifty years of age. They may be present without any evidence of myocardial disease. When the heart is diseased, however, they tend to be frequent. They are associated with the excessive use of tobacco and will sometimes cease on omission of the drug. By themselves, *i.e.*, unaccompanied by cardiac enlargement, degenerated arteries, tachycardia, valvular disease, or other signs and symptoms suggesting myocarditis, they are without significance whether auricular or ventricular. If they occur after or during an attack of chorea or rheumatic fever, or if present along with other and definite evidence of cardiac damage, they may be regarded as almost certainly allied in some way to an underlying inflammation. Not uncommonly they constitute the only clinical warning of an active process invading the myocardium. For example, the persistence of extrasystoles, following an attack of scarlet, rheumatic, or diphtheritic infection, should suggest a prolongation of convalescence until the premature beats are absent or relatively infrequent.

Extrasystoles produce irregularity in the pulse, both in volume and in rate. When very frequent, the irregularity may simulate closely the type of pulse met with during auricular fibrillation or flutter of the auricles. The rate is important in this connection. In heart rates of over 120 per minute extrasystoles are rare, whereas in fibrillation and flutter the irregularity persists when the pulse is raised above 120. This fact provides a simple clinical method of distinguishing between extrasystoles and fibrillation or flutter; mild exercise, sufficient to increase the heart rate to 120, will usually abolish

the irregularity when extrasystoles are responsible, but as the heart rate falls again the irregularity may be intensified. In cases of fibrillation or flutter, exercise will aggravate rather than abolish the irregularity. In persons predisposed to premature beats, fatigue tends to increase their frequency,

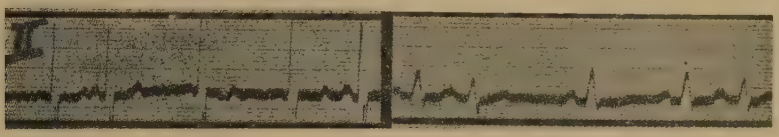

FIG 12

Auricular extrasystoles with practically no compensatory pause, from two elderly men with arteriosclerosis.

(From E.C.G., by Dr Maurice Campbell.)

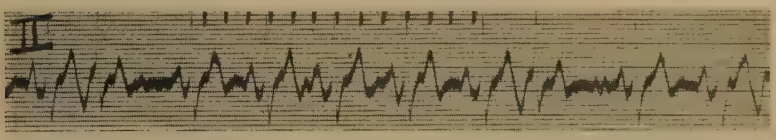

FIG. 13

Auricular extrasystoles arising in the auricle some way from the sino-auricular node and spreading backwards through the auricle as shown by the inverted P waves with each premature beat.

(From E.C.G., by Dr Maurice Campbell.)

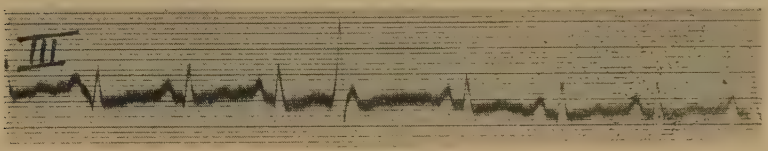

FIG. 14

Nodal extrasystole from an elderly man with atheroma. The P wave can be seen just after the premature beat.

(From E.C.G., by Dr Maurice Campbell.)

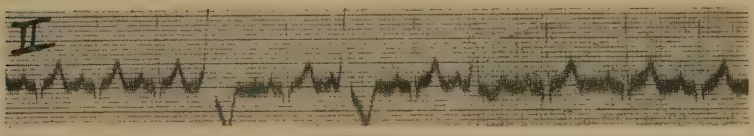

FIG. 15

Ventricular extrasystoles. The second is less premature than the first so that the P wave can be seen just before QRS.

(From E.C.G., by Dr Maurice Campbell.)

particularly during the period of slow pulse and bodily fatigue following excessive exertion. If extrasystoles occur during tachycardia they are an indication of toxic myocarditis.

The character of the heart sounds during an extrasystole will depend on the precise point during diastole at which the extra beat occurs. Should it, for example, occur when the ventricles are comparatively empty, the pulmonary and aortic valves may not open, and consequently there will be only a first sound and no second sound to accompany the extra beat; nor will there be any associated pulse wave at the wrist. Frequent extrasystoles may thus

give rise to a deficiency in the pulse-rate as compared with the ventricular rate in the same ways as during fibrillation. It should be borne in mind that auricular fibrillation is occasionally preceded by frequent extrasystoles for a considerable period.

Extrasystoles do not give rise to any special symptoms, and may pass unnoticed by the patient. In nervous subjects, however, anxiety may result from the sensation of a " thump " or " shock " in the chest that is occasionally felt to follow a premature beat. Normal persons, when resting quietly, may sometimes be conscious of an isolated extrasystole. When, however, they occur in paroxysms which frequently recur or continue for long periods, distress may be marked.

Paroxysmal Tachycardia

This term is applied to tachycardia of limited duration characterised by an abrupt onset and an equally abrupt cessation. It is due to a regular sequence of impulses arising in an ectopic focus in the heart muscle; such a focus may be in the auricles, A-V nodes, or ventricles. In the two former the condition is known as *auricular or nodal paroxysmal tachycardia*, in the last as *ventricular paroxysmal tachycardia*. In all the tachycardia is really a series of extrasystoles.

Ætiology.—Paroxysmal tachycardia of auricular or nodal origin is relatively common. In a large series studied recently more than half occurred

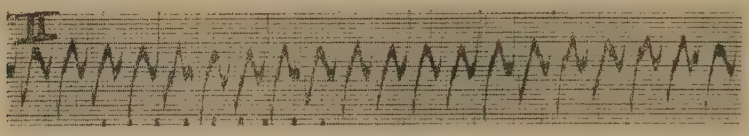

Fig. 16

Paroxysmal auricular tachycardia at a rate of about 200. Alternation in the strength of the ventricular beats can be seen, but this is unusual.

(*From E.C.G., by Dr Maurice Campbell.*)

in otherwise healthy persons without demonstrable evidence of cardiac disease. In many the heart was normal after the paroxysms had been present for twenty to forty years. Paroxysmal ventricular tachycardia, on the other hand, occurs chiefly in association with congestive failure or coronary occlusion. Sometimes it may be brought about by excessive doses of digitalis. Fortunately it is much less common, and the patient with it is generally already under observation because of the condition of the heart. The following description refers only to the more common disorder, namely, the auricular and nodal type.

Symptomatology.—The heart rate during a paroxysm remains remarkably steady at a given level for a given individual. The rates commonly vary between 150 and 200, but may exceptionally be as low as 140 or as high as 240. The ventricles beat at the same rate as the auricles. The pulse-rate during a paroxysm is uninfluenced by changes in posture. An attack may be associated with no unpleasant sensations beyond a fluttering in the chest or throat, or it may give rise to profound distress, including pain over the precordium, a feeling of fullness and distension in the abdomen, flatulent

dyspepsia, nausea and even vomiting, great fatigue, and attacks of fainting. In prolonged attacks the patient becomes cyanosed, and in due course all the signs of severe congestive failure may develop. The severity of symptoms depends on the degree to which the blood pressure falls and the extent of cardiac dilatation.

Paroxysms may occur at long intervals of months or years, or may recur at intervals of days or hours. An attack may last from a few seconds to ten days. In a recent investigation the usual duration of the paroxysms was more often hours than days, but one-third of the patients had paroxysms lasting more than a day, 10 per cent. rarely, 10 per cent. often, and 10 per cent. habitually. They may come on without warning at any time, or be precipitated by a heavy meal, excitement, or other trivial event. A paroxysm ceases abruptly either spontaneously or following change of position of the body, placing the head between the knees, pressing on the eyeballs, holding the breath under pressure, or the act of vomiting. Lewis states that deep

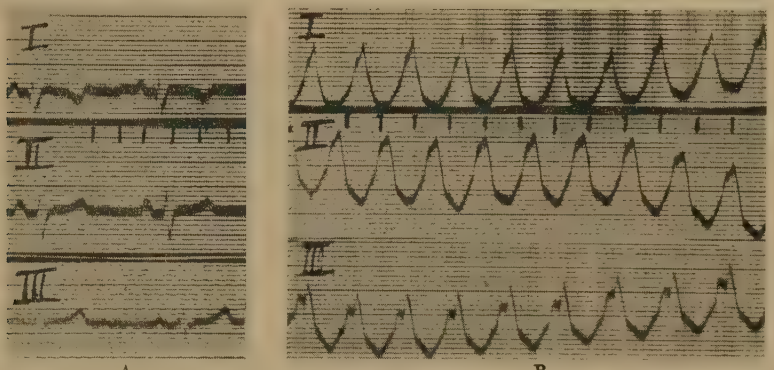

FIG. 17

Paroxysmal ventricular tachycardia, rate 208 (auricular activity hidden), from a man with myocardial disease. A, normal rhythm ; B, paroxysm.

(From E.C.G., by Dr Maurice Campbell.)

pressure below the angle of the jaw over one or other of the carotid arteries, when maintained for 10 to 20 sec., sometimes stops an attack through a reflex of the carotid sinus. Many tricks of sudden movement (*e.g.*, bending down to open a low drawer) may stop an attack ; perhaps a forced expiration with a closed glottis after a deep inspiration is the most generally successful. No measure proves equally efficient in every case, though the same measure is often successful in an individual patient.

The more frequent and prolonged the attacks the worse the anxiety and distress ; a paroxysm lasting more than a few days usually results in severe prostration. If, during the free periods, the cardiovascular system is apparently sound and the exercise tolerance high, and provided the paroxysms are short and infrequent, the prognosis remains good. With evidence of myocardial damage during normal rhythm, such as generalised arteriosclerosis, cardiac enlargement, valvular disease and frequent prostrating attacks, the outlook is poor. For though sudden death in an attack is very rare, frequent attacks superimposed upon an already damaged myocardium must surely increase the rate of myocardial deterioration.

Prognosis and Treatment.—When the paroxysm occurs in a patient who is otherwise healthy, one of the simple procedures described above may sometimes suffice to terminate it.

Paroxysmal tachycardia is a symptom rather than a disease. In a minority of patients, chiefly with ventricular paroxysmal tachycardia, it accompanies serious heart disease, and the prognosis then is grave. In most patients paroxysmal tachycardia is not in itself of any grave significance. It is due to reflex causes more often than to any primary change in the heart muscle. This applies not only to the majority whose hearts are otherwise normal but to most of those with rheumatic heart disease and to some with other myocardial disease. In some of the rheumatic cases, and less often in others, paroxysms of fibrillation may alternate with or replace paroxysms of tachycardia. In the rheumatic cases established fibrillation then becomes a possibility in the near future.

The prognosis of paroxysmal tachycardia as regards life is therefore excellent, unless it is of the rare ventricular type, unless appearing relatively late in life and as the first indication of disease of the coronary arteries, or unless before the paroxysms have started there is already serious heart disease.

During an attack rest should generally be advised, but rest in bed is not needed unless special symptoms, or the condition of the heart at other times, make it advisable. If an attack persists towards evening, bed, with a sedative or hypnotic, will generally lead to its arrest. Quinidine, 5 gr., repeated if necessary in two hours, is probably the most useful medicinal treatment. The cessation of attacks after digitalis has often been reported, but it is doubtful if it is effective, and generally it should not be given unless indicated by the state of the heart apart from the paroxysms, or by the development of failure in a long attack. Of newer remedies mecholyl (acetyl-β-methylcholine), 15 mg. intramuscularly or intravenously, is sometimes successful, but is unpleasant. Prostigmin, 0·5 mg. subcutaneously, has more effect and is harmless to use. Morphine is not desirable in ordinary recurrent attacks.

After the paroxysm the most important question is to determine the condition of the heart. If thorough examination justifies it, reassurance about the nature of the attacks is often all that is called for, and this alone will sometimes greatly diminish their incidence. The general regulation of the patient's life as regards food, work, and exercise must next be attended to, and in many cases a sedative, such as bromide, will be all else that is needed. If, in spite of this, the attacks are frequent and troublesome, regular administration of quinidine for a time, 3 to 5 gr. t.i.d., will often succeed.

Differential Diagnosis.—A regular pulse-rate of 160 or over, paroxysmal in character, is nearly always an indication of paroxysmal tachycardia. In auricular flutter and fibrillation the pulse-rate is usually lower, and in the case of fibrillation there is in addition a striking irregularity. In doubtful cases an electrocardiogram is decisive.

Heart Block

In heart block the power of the conducting tissues to transmit impulses is impaired. Thus there may be a delay in the passage of the impulse from auricles to ventricles ; or, if the block is more severe, only a fraction of the auricular contractions reach the ventricular muscle ; in complete block no

auricular beats reach the ventricles, and auricles and ventricles beat independently. The electrocardiograph reveals minor degrees of block that are clinically unrecognisable ; in such cases a prolongation of the P-R interval beyond the normal limits (0·20 sec.) is the diagnostic feature.

Heart block is invariably associated with damage to the auriculo-ventricular bundle. In young patients the cause is usually a rheumatic or diphtheritic inflammation, or, less commonly, an attack of tonsillitis, but a few instances of heart block of congenital origin have been described. In elderly persons it is due to some form of chronic myocardial disease, most often with atheroma, or it may occur following coronary thrombosis. In both groups autopsy reveals lesions in the junctional tissues ; in elderly persons, particularly, the bundle may be found to be sclerosed, calcified, interrupted by a gumma or neoplasm, or otherwise involved in some gross lesion.

In slight degrees of block isolated auricular beats may fail to stimulate the ventricles, thus giving rise to the so-called " dropped beat." This must be

Fig. 18

A curve of complete heart block, or dissociation of the auricular and ventricular rhythms. The auricles and the ventricles are beating regularly, but at the independent rates of 64 and 29 respectively.

(From E.C.G., by Dr Maurice Campbell.)

distinguished from an extrasystole, in which condition there may be no pulse at the wrist, although the ventricle contracts. In pulsus bigeminus alternate extrasystoles fail to come through to the pulse at the wrist. The condition is often due to digitalis poisoning and is frequently mistaken for the much more serious condition of heart block.

When alternate auricular contractions are followed by ventricular responses, we speak of a 2 : 1 block. This condition is suggested clinically when the pulse-rate is observed suddenly to become halved or doubled. 2 : 1 block is an unstable rhythm, readily disappearing under the influence of excitement, mild exercise, and certain drugs. It is sometimes met with in hyperthyroidism. The preceding examples are known as partial block, for the ventricles are not completely cut off from the auricles. In complete block the two sets of chambers beat independently, the ventricles contracting at their own characteristic rate of below 40. When the heart rate is persistently below 35, it is almost certain that complete dissociation has occurred. In complete block the pulse is regular, of good volume, and unaffected by posture, exercise, or drugs influencing the heart rate, such as amyl nitrite and atropine. Faint muffled sounds representing the auricular beats may be heard in the prolonged diastole, and when ventricles and auricles beat synchronously an unusually loud first sound is heard. In the same way, when auricular systole falls near the first or second sounds, reduplication or accentuation of either of these may be heard. The electrocardiogram (Fig. 18) shows clearly the complete dissociation between P (auricular) and Q, R, S, T (ventricular) complexes.

Since heart block is merely one sequel to a widespread lesion, the symptoms in such cases are those of a progressive myocardial disorder. Although there are many instances on record where patients with complete block have carried on a useful life for many years without unpleasant symptoms, the prognosis is usually poor. It is not the heart block that destroys the patient, but the inevitable cardiac failure eventually resulting from the concomitant myocardial damage and the grave risks arising from Stokes-Adams attacks.

Stokes-Adams Syndrome.—It occasionally happens, and especially during the transitional stage between partial and complete block, that the ventricles fail to beat for a considerable period, or contract at rates (below 10 per minute) insufficient to maintain an adequate cerebral circulation. Syncopal attacks preceded by dizziness ensue, or, when there is prolonged diastole, transient unconsciousness and convulsions. Sometimes sudden death occurs. Such attacks are to be distinguished from minor and major epilepsy, which they may closely resemble ; they are, however, much shorter in duration. The characteristic slow pulse should settle the diagnosis. Patients with heart block are likely to develop Stokes-Adams attacks soon after its onset or not at all.

The treatment of heart block, whether partial, complete, or complicated by Stokes-Adams attacks, calls for no special measures beyond those required for chronic heart disease (*vide* p. 415). Intracardiac adrenaline may restart a heart which has stopped, and ephedrine ($\frac{1}{2}$ gr. t.d.s.) may diminish the frequency of Stokes-Adams attacks.

Bundle Branch Block.—This cannot be diagnosed except by the electrocardiographic changes, though it may be suspected sometimes in patients

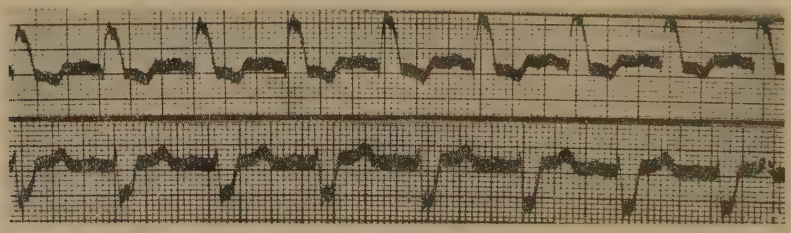

Fig. 19

Left bundle branch block, leads I and III. The QRS complexes are widened and notched and the T waves are in the opposite direction to the main deflection, making it biphasic. The R wave in lead I, and the S wave in lead III, indicate the divergent type, which is left bundle branch block. A similar S wave in lead I, with an R wave in lead III, would indicate right branch block.

(*From E.C.G., by Dr Maurice Campbell.*)

with heart failure with pulsus alternans, gallop rhythm and a rather bifid apex beat. In left bundle branch block there is a picture of extreme right ventricular preponderance with the R or S waves wide and notched and the T wave opposite to these making a biphasic complex. The opposite picture is seen in right bundle branch block. It may occasionally be of relatively little significance but usually it is found with grave heart disease, generally with a bad prognosis, and there is considerable risk of sudden death. A large heart with failure and past or present high blood pressure is perhaps the commonest underlying cause.

Auricular Flutter

Auricular flutter is a condition in which the auricles beat at a much increased rate in a highly abnormal manner. Lewis has shown that in flutter "the contraction wave follows a circular and never-ending path in the auricle, the complete circuits being accurately repeated usually from 260 to 320 times per minute in different subjects." The diagnosis is difficult on clinical examination alone, but may be suspected when a rapid heart rate persists at an extremely regular rate for longer than would be expected with paroxysmal tachycardia, or when the heart appears fast and regular at one moment and completely irregular a moment later. An electrocardiogram shows the increase in the rate of the auricular contractions by the presence of an increased number of P waves. In flutter, the ventricles rarely contract at the same rate as the auricles, and it is usual to find some degree of heart block reducing the ventricular rate to some simple fraction of the auricular, such as 1 : 2, or, less commonly, 1 : 4. In about one-third of the cases the degree of heart block is

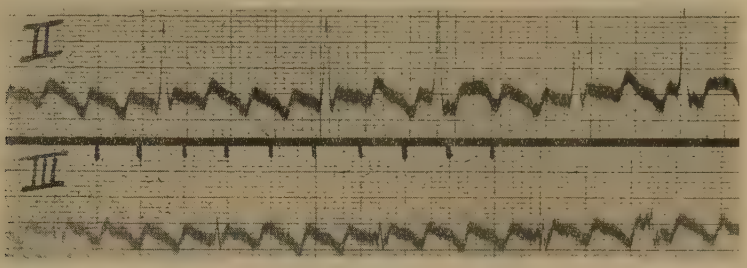

Fig. 20

Auricular flutter. In lead II the ventricular rate is irregular as the A-V block varies between 3 : 1 and 4 : 1. In most of lead III the rate is regular as the block is 4 : 1. Flutter is generally seen easily in leads II and III but less obvious in lead I.

(*From E.C.G., by Dr Maurice Campbell.*)

frequently changing and the heart rate is then irregular and is very hard to distinguish from auricular fibrillation.

Nothing is known of the underlying cause. Flutter may occur at any age, but is most commonly observed during or after middle life. The ætiological factors are the same as in auricular fibrillation (*vide* p. 384).

Symptoms and Diagnosis.—Auricular flutter occurs in paroxysms, or may persist for life unless it change to fibrillation under the influence of digitalis. The symptoms of paroxysmal flutter and paroxysmal tachycardia are very similar. The ventricular rate in flutter is seldom as rapid as in paroxysmal tachycardia and is usually between 130 and 160. When the patient is at rest it may fall conspicuously and become noticeably irregular.

Occasionally instances of persistent flutter show little discomfort, but this is rare. Patients with a poor exercise tolerance during normal rhythm are much upset by the onset of flutter, and evidence of rapid congestive failure may arise. Whenever the ventricles take on the full auricular rate, a rare event, profound distress or even unconsciousness may supervene.

Prognosis and Treatment.—The prognosis, as in almost all cardiac disorders, depends on the condition of the myocardium. The presence of arteriosclerosis, valvular disease, high blood pressure, and other complications

such as nephritis, or anæmia, must all be taken into account. Treatment should be directed towards minimising the work of the heart. The drug of choice is digitalis, to which, properly administered, there are no contra-indications. Under its influence the flutter may continue without change, or give way to fibrillation. On omitting the drug, the fibrillation may cease and be replaced by normal rhythm. When the flutter persists, digitalis slows the pulse with marked benefit. If digitalis fails to restore normal rhythm and if the case is otherwise suitable (see p. 386) quinidine should be tried and may be effective. If congestive failure is present the patient must, of course, be confined to bed and suitable measures employed.

Auricular Fibrillation

With the exception of extrasystoles, auricular fibrillation is the most common, and by far the most important, of the arrhythmias. It is a condition in which there is no synchronised and orderly contraction of the auricular muscle. Individual groups of muscle fibres contract intermittently, frequently, and independently. Lewis ascribes the condition to a wave of contraction coursing continuously, and by different paths, round the auricle at a rate of over 400 cycles per minute, thus differing only in degree from the allied condition of flutter. The fibrillating auricles dilate and do not contribute to the passage of blood into the ventricles. This dilatation occasionally leads to intra-auricular clotting, with grave danger of embolism, either pulmonary or systemic (*vide* p. 440).

The junctional tissues fail to transmit to the ventricle the great majority of the auricular impulses ; only a fraction are effective in producing ventricular contractions, which occur at irregular intervals. It is assumed that in all cases of fibrillation there is some degree of heart block, and it is by increasing this block that digitalis produces its beneficial effect in slowing the ventricular rate.

Ætiology.—Auricular fibrillation, whether paroxysmal or permanent, may be a feature of almost any form of heart disease. Before middle age its incidence is greatest as a sequel of *rheumatic carditis*, and it is particularly common in patients with mitral stenosis. Rarely seen before sixteen years of age, its incidence rises with age, and when congestive failure occurs in the subjects of rheumatic heart disease, fibrillation is the rule. In later life, however, it is a common complication of any form of myocardial insufficiency, particularly that due to the fibroid and fatty changes associated with generalised arteriosclerosis, hypertension, chronic nephritis, and disease of the coronary vessels. Hyperthyroidism is a particularly important factor in the causation of fibrillation and should be suspected in all unexplained cases after middle age. Rarely in acute infections such as pneumonia or cystitis there may be an isolated paroxysm of fibrillation, which is usually of short duration. In a small percentage of cases paroxysmal fibrillation may occur without obvious cause.

Diagnosis and Symptoms.—Fibrillation may be either paroxysmal or permanent. Paroxysmal attacks usually last only a few hours and seldom persist for more than three or four days, and the longer the individual attacks last, the greater the probability of fibrillation becoming permanently established. As a general rule, an attack continuing for a week is likely to continue indefinitely unless terminated by quinidine.

The onset of fibrillation is sometimes preceded by frequent extrasystoles, and a careful watch is necessary to detect the change over from one arrhythmia to the other. The important and characteristic feature of this condition is the complete irregularity of the pulse both in volume and rhythm. This irregularity is usually detected with ease, except when the pulse-rate is unusually low and the heart beats evenly spaced. When the pulse is both rapid and irregular, fibrillation should always be suspected. When it supervenes in a heart with mitral stenosis, the typical crescendo presystolic murmur in the majority of cases disappears, and a low-pitched rumbling diastolic murmur remains to indicate the stenosis. Since the auricles do not contribute to the blood flow into the ventricles, the ventricular output is related to the length of the diastolic pause. After a particularly short diastole there may be insufficient blood in the left ventricle to produce a pulse in the radial artery,

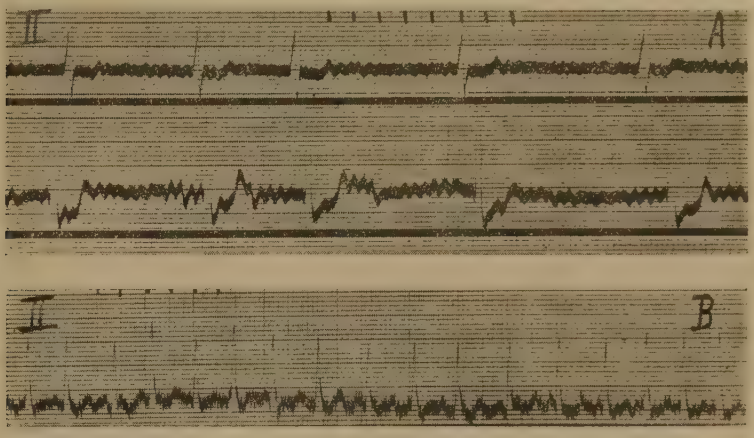

FIG. 21

Auricular fibrillation, showing irregularity of the ventricular rate: no P waves are visible but there are small oscillations. A, At a relatively slow rate after digitalisation. B, At a fast rate and therefore less irregular than usual: before treatment with digitalis.

(From E.C.G., by Dr Maurice Campbell.)

hence the characteristic *pulse deficit*, *i.e.*, the difference between the pulse-rate at the wrist and the heart rate as counted over the precordium. The electrocardiogram displays no recognisable P waves, and the Q, R, S waves are unequally spaced (*vide* Fig. 21).

As in all cardiac disease, the symptoms depend mainly on the efficiency of the myocardium, which is much reduced by an excessive rate due to fibrillation of the auricles. It is noteworthy how seldom fibrillation is accompanied by cardiac pain. In a large number of persons dying of progressive cardiac failure, fibrillation of the auricles appears sooner or later, and unexpectedly sudden death may perhaps be due to the fibrillation affecting the ventricles also. The differential diagnosis of auricular fibrillation and frequent extrasystoles has been discussed on page 376.

Treatment and Prognosis.—The reputation of digitalis as a cardiac tonic was derived from its efficiency in the treatment of fibrillation. By its action in diminishing the conductivity of the bundle of His, the ventricles are shielded from the frequent and irregular impulses originating in ectopic foci in the

auricles. Their rate slows down, the coronary circulation improves, and the efficiency of the myocardium is enhanced with marked improvement in the circulation. Under its influence in cases of advanced failure the output of urine is greatly increased, dyspnœa diminishes, cyanosis becomes rapidly less marked, and mental symptoms disappear.

There is no evidence that digitalis can cause fibrillation to revert to a normal mechanism. Quinidine, on the other hand, in a proportion of cases of established fibrillation, quite definitely brings about a sudden change to normal rhythm, but only a small proportion of cases are suitable for this treatment (*vide* p. 387).

Many cases of established fibrillation have been observed for ten or more years, without apparent deterioration. Their exercise tolerance, however, remains consistently low. Such persons are best kept on small doses of digitalis, suitably spaced, to keep the ventricular rate at an optimum level.

Whereas, in established fibrillation, treatment with digitalis should always be tried, it must be remembered that in paroxysmal fibrillation its effect may be to render the arrhythmia permanent. Except in the rare cases where this is desirable, digitalis should be avoided and an attempt made to terminate the paroxysms by means of quinidine, which may have to be given over a long period (*vide* p. 388). Most paroxysms of fibrillation, however, cease without treatment, but quinidine, given regularly in doses of 5 gr. thrice daily, may assist in diminishing the frequency of attacks or lead to their total disappearance.

Administration of Digitalis and Quinidine.—The effect of digitalis on any tachycardia except that due to fibrillation or flutter is doubtful. It is frequently prescribed with alleged good results in many conditions associated with an acute or chronic myocarditis. It is, however, chiefly in auricular fibrillation with tachycardia that its value is outstanding.

The guide to the dosage of digitalis is the heart rate and the relief of symptoms. Its administration should aim at keeping this at an optimum level in the region of 70 to 80. When the rate falls below this level, symptoms of intoxication such as nausea, vomiting, diarrhœa, and headache may appear. The pulsus bigeminus, in which every alternate contraction is an extrasystole, is characteristic of digitalis poisoning, and the appearance of coupled beats is always an indication to withhold the drug, which has a cumulative action. In feverish patients it is unwise to reduce the pulse-rate below 90 to 100, slight tachycardia being a normal accompaniment of pyrexia. To continue the drug in the face of warning signs may lead to sudden death from direct cardiac poisoning.

Dosage.—Most preparations of digitalis are standardised by biological assay in terms of international units. Powdered digitalis leaf (1 gr.) and tincture of digitalis (10 minims) are equivalent according to this standard, but there is so much variation in each patient, mainly owing to the different amounts that can be excreted in twenty-four hours by the kidneys, that the correct dosage has to be found in each case. Difficulties also arise because many days elapse before an effective concentration in the blood is reached with most preparations of digitalis, and the amount that can safely be given to an ill patient who has not had any previously is very different from the amount that is needed regularly.

When a patient who has not been given digitalis has auricular fibrillation and congestive failure or other indications for digitalis therapy, it may be

urgent to get him under control within as few hours as possible. The best method of achieving this is by the use of digoxin, a preparation containing the alkaloids of digitalis. The initial dose is 0·75 mg. intravenously or 1·5 mg. by mouth ; further doses of 0·25 mg. can be taken by mouth three hourly or at longer intervals. This is safer than massive digitalisation with the tincture and safer and much more effective than intravenous strophanthin ; with the latter the effective dose and the toxic dose are so close that it is often difficult to get any useful control without producing vomiting.

When it is less urgent to get full control at the earliest possible moment, or when a small dose of digitalis has been given ineffectively, a single dose of 1 to 1½ drachms of the tincture may be given, followed six hours later by 20 minims t.d.s. until the full effect is obtained. Small doses may then suffice and be carried on over long periods. When a patient has been fully digitalised the object is to find the optimum maintenance dose, *i.e.*, enough to get the best possible control of the heart without giving rise to toxic symptoms. The authors have found in practice that 12½ minims of a good tincture, or 1 gr. of powdered digitalis leaves, 0·25 mg. digoxin, or $\frac{1}{60}$ gr. of Nativelle's digitaline may be taken as equivalent, and in an average case the dose needed is this amount three times a day. It will be noted that these equivalents found useful clinically are not quite the same as those quoted from pharmacological standardisation on animals. There are, of course, many preparations nearly or quite as good, but the important thing is that the practitioner should confine himself to a small number of digitalis preparations so that he can become really familiar with them. It is important to realise that in fibrillation digitalis generally needs to be continued for the rest of the patient's life.

Some patients show an idiosyncrasy to digitalis, as shown by vomiting after small doses ; in this event Nativelle's digitaline or digoxin may be better tolerated.

Quinidine may be used in an attempt to abolish fibrillation, providing the following contraindications have been excluded :—

(*a*) Idiosyncrasy to the drug, as shown by rashes or by distressing symptoms, such as vomiting and tachycardia, following an initial trial dose of 3 gr.

(*b*) The presence of venous engorgement or congestive failure as shown by cyanosis, œdema, enlarged liver, or dyspnœa.

(*c*) A history of continuous fibrillation for six months or over.

(*d*) Considerable enlargement of the heart (more than 14 cm. maximum transverse diameter in a patient of about 10 stone).

(*e*) A history of recent hæmoptysis and pleurisy, suggesting pulmonary embolism of intracardiac origin, or a history of a systemic embolism, *e.g.*, an attack of hemiplegia.

Quinidine has an important place in the treatment of auricular fibrillation —provided the cases are carefully selected. The ordinary patient seen in hospital is quite unsuitable ; the risk is too great, and if fibrillation is arrested it generally returns soon. Satisfactory results are obtained by paying attention to three main criteria : the absence of congestive failure, of a greatly enlarged heart, or of a long history of fibrillation.

The case is eminently suitable for treatment with quinidine and should certainly be given this opportunity of regaining normal rhythm, if there have been no signs of failure, and if the heart is only slightly enlarged (less than

13 cm. maximum transverse diameter in a patient of about 10 stone), and if fibrillation has been established less than one month.

When there is mitral stenosis these conditions must be strictly observed. Least attention need be paid to them if fibrillation is due to a goitre, as, if necessary, partial thyroidectomy will convert an unfavourable case into one favourable for quinidine.

On the first day of treatment with quinidine one 5-gr. tablet is given, preferably in the morning. On each successive day an additional 5 gr. is given two hours after the previous dose, but the amount should rarely exceed a total of 30 gr. in twenty-four hours. The drug is best given in 5-gr. doses at two-hourly intervals owing to the fact that it is very rapidly excreted. A careful watch must be kept for signs of poisoning, as evidenced by an untoward increase in the ventricular rate. There is no knowing how long normal rhythm may continue when it does appear. In many cases the quinidine is without effect. Rarely fibrillation will revert to normal rhythm within a few hours of a single dose.

Pulsus Alternans

When the radial pulse is alternately weak and strong, though regular in time, it is described as pulsus alternans. It is to be distinguished from an alternate weak and strong pulse, separated by shorter and longer intervals, that is characteristic of alternate extrasystoles, *i.e.*, the pulsus bigeminus. Pulsus alternans may be readily felt on ordinary palpation, but its character is best demonstrated by slowly inflating the sphygmomanometer cuff and observing that, at a certain critical level, the pulse at the wrist becomes exactly halved. Pulse tracings also demonstrate its alternating character. The electrocardiogram shows either nothing of note or, rarely, a corresponding alternation in the amplitude of the R waves. The importance of the phenomenon lies in the fact that it is frequently associated with advanced myocardial disease with an ominous prognosis.

It may be observed in association with high pulse-rates, as in paroxysmal tachycardia; when found at ordinary rates, persistent high blood pressure, arteriosclerosis, renal disease, or angina pectoris are usually present, and it is often noticeable with gallop rhythm (*vide* p. 403). Rarely it is seen in digitalis therapy with large doses.

CARDITIS

By the term "carditis" is meant an inflammatory process involving the myocardium, pericardium and endocardium. Although obvious morbid changes may not be present throughout all the tissues of the heart, there is in most cases more than a localised lesion of one particular portion. Thus rheumatic pericarditis is always associated with some degree of myocarditis, and endocarditis does not arise as a separate entity apart from damage to the myocardium. It is therefore permissible to employ the term "carditis" in a wide sense to imply an inflammation of the heart, whether it involves the myocardium alone, or in addition the endocardium and pericardium.

Having emphasised the fact that there is a close relationship between all inflammatory processes which involve the various tissues of the heart, it is now permissible to deal individually with affections of the muscle, the pericardium, and the endocardium. Of these, perhaps the most important is

myocarditis, as it is primarily upon the adequate functioning of the heart muscle that life depends. Moreover, in every inflammatory condition of the heart the myocardium is invariably affected.

ACUTE MYOCARDITIS

The pathological changes found in myocarditis have been mainly studied in acute rheumatism. The most striking gross change is enlargement of the heart, particularly of the ventricles; thus the heart may be found to be both larger and heavier than normal. As a result of the process of dilatation, the auriculo-ventricular orifices are wider than normal. Histological examination shows localised collections of large branching cells with multiple nuclei and an admixture of lymphocytic cells; these are termed "Aschoff's bodies" or submiliary nodes, and occur in the heart muscle around the smaller arterioles, particularly under the endocardium and the pericardium. In other infections, such as diphtheria or scarlet fever, the changes are not so characteristic as in rheumatic fever, but the muscle cells show evidence of an acute inflammatory process, with infiltration of round cells and leucocytes.

Myocarditis produces no typical physical signs. Displacement of the apex beat to the left will indicate increasing enlargement, and the apex beat may become diffuse. The first sound may change in quality and become fainter, often a point of considerable diagnostic importance. A systolic murmur is often present. Sometimes, too, there is an absence of symptoms, and the heart may have been considered to be unaffected until sudden failure occurs, sometimes even during convalescence, as may occur in diphtheria. In some cases involvement of the myocardium may be suggested by persistent tachycardia, by various arrhythmias, such as extrasystoles, or occasionally by bradycardia. In severe myocarditis sudden death may occur, or there may be symptoms of congestive cardiac failure with cyanosis, œdema, and dyspnœa. The recognition of myocarditis is of extreme importance, and in the affections which are specially liable to attack the heart, great care must be taken to allow an adequate period of rest. It is equally important not to make a diagnosis of myocarditis in those with only nervous symptoms.

PERICARDITIS

Rheumatic pericarditis is relatively rare, and its occurrence always signifies grave involvement of the myocardium. Apart from rheumatic fever, it may arise in tuberculosis, where it is not so uncommon as was formerly thought, and in pneumonia and septic infections, such as osteomyelitis and pyæmia. In the young, acute rheumatism and osteomyelitis are the chief causes, but it also occurs in older persons as a terminal infection in chronic diseases, particularly nephritis. Pericarditis is often a feature of infarction of the myocardium. In tuberculous and malignant pericarditis a blood-stained effusion is not uncommon.

Pericarditis may or may not be accompanied by an effusion, but there is no justification for drawing any sharp distinction between a simple fibrinous pericarditis and that in which there is also a pericardial effusion, as the basic pathological process is similar, although the physical signs produced are very

different. The normal smooth glistening surface of the pericardium becomes roughened by the exudation of lymph, which coagulates and forms a fibrinous layer over the heart. The process may involve only localised areas in the pericardium, but frequently it is more generalised; in the milder cases there is little or no effusion, but often the pericardium becomes gradually distended with fluid which may be serous, blood-stained, seropurulent or purulent. When pericarditis is extensive, the pericardium is very much thickened with a rough and shaggy surface. If the patient survives the acute stage, organisation of the coagulated lymph takes place, and the visceral and parietal layers of the pericardium may become firmly adherent together, and thus produce the condition known as adherent pericardium.

Physical Signs and Symptoms of Pericarditis.—Pericarditis occurs secondarily to disease elsewhere in the body, and often the symptoms are overshadowed by those of the primary disease. This is specially true in the terminal pericarditis associated with chronic nephritis, when it is not uncommon to find unsuspected pericarditis at autopsy. The onset of pericarditis may be associated with precordial pain, which is often aggravated by coughing, deep breathing, or movement. With pericardial effusion, dyspnœa, restlessness, and insomnia are often marked features; the distress is more striking when the effusion has collected rapidly. When the effusion is purulent, as in pyæmia, the skin is ashy-grey in colour, and the patient is obviously extremely ill.

On physical examination in the early stages the heart is found to be enlarged, and occasionally fremitus may be felt; a friction rub is heard which is to and fro in character, corresponding with systole and diastole. The intensity of the rub varies considerably in individual cases, and from time to time in the same case. It is harsher and more grating in character than a to-and-fro valvular murmur, sounds close to the ear, and often becomes louder on pressing the stethoscope firmly against the chest. As rheumatic pericarditis occurs mainly in severe carditis, there is necessarily an associated involvement of the heart muscle.

With the development of a pericardial effusion there is a marked change in the physical signs; a rub previously audible over the whole precordial area may disappear completely as the layers of the pericardium become separated by fluid; more often, however, it may still be heard over the base of the heart when the patient is examined lying down, as the fluid gravitates to the back of the pericardial sac; the area of cardiac dullness is increased and, with a large effusion, assumes a characteristic pear-shaped form with the apex pointing upwards; the dull area extends to the right of the sternum; the apex beat becomes more diffuse or may disappear completely, and the sounds become muffled and indistinct. The percussion note over a pericardial effusion is very dull and "board-like," thus resembling that heard over a pleural effusion. An X-ray examination is of great value. The heart shadow occupies a median position in the thorax, and the shadow cast to the right of the spine is often as large as that on the left side.

The presence of a pericardial effusion may be established by exploratory puncture. The most satisfactory site is a point in the fifth left interspace about 1 in. internal to the outer limit of the cardiac dullness. A wide needle is used and is inserted slowly, unattached to a syringe; if the needle comes in contact with the heart this will usually become immediately apparent by the movement of the needle with each cardiac systole. Most physicians must,

however, at some time have had the somewhat alarming experience of exploring the cavity of the ventricle while attempting paracentesis of the pericardium. There is no difficulty in the recognition of such an accident, as blood spurts out through the needle at each heart beat. Strange to relate, even when pierced by a needle the heart may continue to beat normally, and on withdrawal the muscle of the ventricle immediately closes the perforation.

Treatment.—Pericarditis without effusion calls for no special treatment other than that required for the underlying condition. If, however, a large effusion is present this may produce severe respiratory distress, which can only be relieved by aspiration. In tuberculous pericarditis, fluid accumulates rapidly and large amounts may need to be aspirated at frequent intervals. With purulent effusions, as for instance those associated with osteomyelitis or pneumococcal infection, penicillin is essential, given both parenterally and by injection into the pericardium (*vide* p. 9). Surgical drainage may be required in addition.

Prognosis.—In pericarditis of rheumatic origin the prognosis depends on the associated damage to the heart muscle and valves and complete recovery is unusual. On the other hand, in pericarditis associated with osteomyelitis and pyæmia, the heart muscle is much less affected, and if the patient survives the ultimate outlook is good.

Adherent Pericardium and Constrictive Pericarditis

Following acute pericarditis, whatever its cause, the visceral and parietal layers of the pericardium may become adherent and in addition in some cases adhesions may form between the adherent pericardium and surrounding structures, such as the pleura, diaphragm, and chest wall. This may result in the heart being enclosed in a thick fibrous casing, which in the course of time may become to some extent calcified. Adherence between the layers of pericardium alone is unlikely to cause symptoms and is usually only detected as a chance finding at autopsy. If, however, the pericardium is much thickened and becomes adherent to other structures, the contractions of the cardiac muscle are restricted. Moreover, the thickened pericardium often obstructs the entry of venous blood, chiefly from the inferior vena cava, thus producing back pressure in the liver and lower limbs with resulting œdema and ascites. This condition is termed *constrictive pericarditis.*

Although rheumatic fever is the most frequent cause of acute pericarditis it is rare for it to produce symptoms which can be ascribed to constrictive pericarditis. Most patients with constrictive pericarditis have no rheumatic history and have often had no obvious cardiac disease until in early adult life they begin to develop increasing dyspnœa which is followed by œdema of the legs, ascites with hepatic enlargement, and sometimes pleural effusions. Examination, clinical and radiological, usually shows no cardiac enlargement and sometimes in an X-ray calcification of the pericardium may be visible. The apex beat and the position of the heart are fixed, *i.e.*, there is no shift with change of posture. Constrictive pericarditis should be suspected when a previously healthy adult below middle age insidiously develops dyspnœa and œdema.

The clinical syndrome of hepatic enlargement with ascites, œdema, and pleural effusions was described by Pick nearly fifty years ago and is often

known as Pick's disease. Some of these cases were probably constrictive pericarditis.

Few if any cases are due to rheumatic fever; tuberculosis is responsible for some cases, but in some the ætiology is unknown.

Following rheumatic pericarditis the layers of the pericardium may become adherent, but it is probable that subsequent symptoms of cardiac insufficiency are due to myocardial and valvular lesions rather than the adherent pericardium.

Medical treatment in constrictive pericarditis is of little avail, but striking improvement may result from resection of as much of the thickened pericardium as is possible. As the outlook without surgery is bad it is justifiable to advise operation, especially if the pericardium is shown to be calcified.

Various physical signs have been described as indicating an adherent pericardium: a diffuse apex beat, fixity of apex beat, systolic retraction of the precordial intercostal spaces, and Broadbent's sign (systolic retraction of the chest wall overlying the eleventh and twelfth ribs). None of these are pathognomonic of the condition. It is probable that except in constrictive pericarditis the symptoms ascribed to adherent pericardium are due to other causes such as rheumatic myocarditis and valvular lesions with great cardiac enlargement.

ENDOCARDITIS

By the term "endocarditis" is meant an inflammatory condition affecting the lining membrane of the cavity of the heart; occasionally the endocardium covering the muscular wall of the heart is involved, and such a condition is described as *mural* endocarditis, but more often the inflammatory process is confined to those folds of the endocardium which form the valves. Endocarditis involving only the valves on the right side of the heart is rare, apart from congenital heart disease.

Much confusion has arisen as regards the nomenclature of endocarditis, owing to the fact that terms are often used in different senses by various authors. All forms of endocarditis are almost certainly infective, yet the term "infective endocarditis" is often limited to a special type characterised by ulceration of the valves and multiple embolic phenomena. This special type is best described under the heading of bacterial endocarditis.

From a clinical and pathological point of view endocarditis may be grouped into four types :—

1. Simple endocarditis, almost always due to rheumatic infection and part of a general carditis.
2. Acute bacterial endocarditis, which is due to infection by the staphylococcus, hæmolytic streptococcus, pneumococcus, gonococcus, or other organisms.
3. Subacute bacterial endocarditis, due to the *Streptococcus viridans*.
4. Syphilitic aortitis spreading to the aortic valve.

In simple endocarditis no micro-organisms can be cultivated from the valves, and there is a tendency toward the development of chronic fibrotic changes. The second type, acute bacterial endocarditis, which was always fatal before the advent of penicillin, is but one manifestation of a general acute septicæmic process due to invasion of the blood by bacteria. The third type, subacute bacterial endocarditis, is midway between the other two

in so far that attempts at healing may sometimes occur, and it is nearly always associated with one specific type of organism, the *Streptococcus viridans*.

Before attempting separate descriptions of these three types of endocarditis, it is necessary to emphasise certain features which are common to all three varieties. It has already been stated that endocarditis affects mainly the valves on the left side of the heart, except in congenital heart disease. The tricuspid valve, however, is often found to be involved in conjunction with a mitral and aortic endocarditis.

The earliest pathological changes in endocarditis are the formation of small elevated areas along the line of closure of the valves; these are known as vegetations. In the simple or rheumatic type these vegetations are generally small, as a rule a few millimetres in diameter, but in acute and subacute bacterial endocarditis they are often large and friable. The vegetations are composed of blood platelets and fibrin deposited upon the swollen endothelium; sometimes it is possible to isolate micro-organisms from the vegetations, but in many cases, and always in simple endocarditis, blood culture is negative, and no organisms can be recovered from the local lesions; it may be assumed that toxins produced elsewhere may lead to degenerative changes in the valve and, as a result, to the deposition of fibrin from the blood.

Simple Endocarditis

Acute rheumatism accounts for the great majority of cases of chronic valvular disease which result from acute endocarditis. It is true that sometimes patients with evidence of endocarditis are encountered who give no history of either rheumatism or chorea, but in such cases it must be remembered that the joint manifestations of acute rheumatism in childhood may be readily overlooked. Indeed rheumatic carditis is not uncommon without obvious joint symptoms. It is possible, however, that other infections, particularly scarlet fever or repeated attacks of tonsillitis, may produce an endocarditis resembling that produced by rheumatic infection.

In simple endocarditis associated with rheumatic fever microscopical examination of the deeper part of the affected valves reveals the presence of aggregations of cells similar to those described in the cardiac muscle under the term "Aschoff's bodies." With the subsidence of the acute infection, the vegetations become the seat of a process of slow fibroid change continuing for many years. This results in the valve segments becoming deformed, producing incompetence or stenosis.

Symptoms and Signs of Simple Endocarditis.—It has already been stated that endocarditis is but one aspect of a carditis, and that its presence implies associated myocarditis and sometimes pericarditis. It is not surprising, therefore, to find that any symptoms due to endocarditis are usually overshadowed by those referable to the inflammation of the heart as a whole. In other words, the diagnosis of endocarditis is necessarily speculative in the earlier stages of an illness such as rheumatic fever, and its occurrence may only be definitely proved by the development, at a later stage, of chronic valvular disease. Certain physical signs may, however, be present, and either prove or suggest the presence of valvular involvement. Thus the detection of an early diastolic murmur over the base of the heart, or down the sides of the sternum, is definite evidence of an aortic valvular lesion. A decision as to

involvement of the mitral valve is not, however, equally easy. It has already been pointed out that in many normal persons systolic murmurs are frequently heard in the absence of mitral disease (*vide* p. 373). A systolic murmur at the apex may be produced by a widening of the mitral ring resulting from dilatation of the left ventricle, such as may occur in any form of myocarditis. It is difficult to distinguish a murmur so produced from one associated with the presence of actual vegetations on the valve cusps. Often, indeed, the ultimate decision must be left in abeyance until the development of other signs of a mitral lesion prove the valve cusps to be involved. It is sometimes stated that apical systolic murmurs due to simple dilatation of the heart are more localised than those due to mitral endocarditis, whereas those due to the latter condition are likely to be propagated into the axilla. This, however, is not always true. Although, therefore, the development of an apical systolic murmur even in the course of rheumatic fever cannot be regarded as definite evidence of a valvular lesion, it must necessarily be viewed with grave suspicion, and is an indication for prolonged and complete rest.

Mitral endocarditis should never be diagnosed on the strength of a systolic murmur alone. Enlargement of the heart, however, associated with a systolic murmur, strongly suggests that the valve has not escaped. An erroneous diagnosis of organic heart disease may affect irreparably the well-being of the patient, in that exercise and the normal activities of life may be unnecessarily restricted.

As simple endocarditis is merely one manifestation of a carditis, it calls for no special treatment apart from that necessary in any case where inflammation of the heart is present. In acute rheumatic endocarditis, embolism is rare, though it occurs frequently in chronic valvular disease, particularly when auricular fibrillation or subacute bacterial endocarditis are present.

Acute Bacterial Endocarditis

In this type of endocarditis, vegetations are found upon the valves as a result of a general blood infection with varying types of organism, such as pneumococci, streptococci, staphylococci, or gonococci. The involvement of the valves is but one feature of a more generalised bacterial invasion of the tissues, and is often but a terminal manifestation. Unlike simple endocarditis, the acute bacterial type shows no tendency towards fibrosis or healing. The clinical picture is that of a pyæmia, and the endocarditis is usually a complication of osteomyelitis, pneumonia, multiple abscesses, or suppurative arthritis. Fortunately the condition is relatively uncommon, and the outlook has improved as the result of intensive chemotherapy.

Subacute Bacterial Endocarditis

This type of endocarditis is practically confined to patients with a pre-existing valvular lesion, nearly always rheumatic but occasionally congenital. Even a bicuspid aortic valve may predispose to infection. The clinical features and course are extremely variable. In its most frequent form the illness starts as a general malaise with slight fever, often thought to be influenza. The temperature fails to subside, but examination may reveal nothing beyond a valvular lesion known to have been present for many years.

The complexion is sallow, and there is an anæmia of microcytic type with a moderate leucocytosis. Night-sweats are frequent, and there is often a slight loss of weight. Petechial hæmorrhages may usually be seen at some stage of the disease occurring spontaneously in the skin and mucous membranes. A blood culture at this stage may produce a growth of *Streptococcus viridans*, or the cultivation may be negative at the first attempt, though ultimately positive cultures can nearly always be obtained. After a variable period, symptoms of embolism occur; in some cases there is pain in the extremity of a finger or toe, accompanied by redness and swelling, indicating the blocking of an arteriole by an embolus; similar indurated and tender areas occurring in the skin are known as Osler's nodes. The spleen becomes palpable, and there may be abdominal pain due to perisplenitis over a splenic infarct. Albuminuria or hæmaturia indicate either embolic nephritis or infarction of the kidneys. A somewhat rare occurrence is embolism of the central artery of the retina, which produces sudden and complete blindness in the affected eye. Examination shows pallor of the fundus with a bright cherry-red spot at the macula. Embolism of mesenteric vessels may produce acute abdominal symptoms. The pyrexia continues, though occasionally for a few days it may be absent, usually without obvious improvement in the general condition. The fingers sometimes become clubbed. The heart often enlarges, sometimes very rapidly. There may be a change in the character of the murmurs, or evidence of the involvement of a valve previously thought to be unaffected. After a variable period, usually not less than six or more than twelve months, death occurs, sometimes from heart failure and exhaustion, sometimes as the result of uræmia due to an acute focal nephritis, or sometimes from cerebral embolism.

Less typical forms of the disease than that described above may lead to great difficulty in diagnosis. In some cases the onset is relatively acute, and the clinical features of the case may suggest typhoid fever; in others the disease may be almost latent with but slight and occasional pyrexia. In spite of the fact that infected emboli are being discharged into the arterial circulation in large numbers, suppuration does not occur.

The signs and symptoms of subacute bacterial endocarditis are dependent on two main factors, the septicæmia and the embolic phenomena. The character of the disease depends in part upon the virulence of the infection and the extent and localisation of the infarcted areas. Among the symptoms resulting from the septicæmia are pallor and anæmia, pyrexia, and splenic enlargement, while the embolic side of the disease gives rise to a number of focal lesions, both in the skin and viscera. Libman lays great stress on the importance in diagnosis of petechiæ in the skin and conjunctivæ and a brownish pigmentation of the face, which is common in the later stages of the disease. He has also shown that in a certain proportion of cases bacteria disappear from the blood. Such a condition he terms the bacteria-free stage. Unfortunately, however, the transition to this stage does not mean that the patient necessarily recovers, as the damage wrought by emboli remains and frequently results in death from uræmia due to focal glomerular nephritis. Attempts at healing often produce still further aggravation of the old valvular lesions, with resulting myocardial failure. It is remarkable how seldom fibrillation and subacute bacterial endocarditis occur in the same patient.

In subacute bacterial endocarditis the vegetations are most often confined to the mitral and aortic valves, and destruction of the valve by ulceration

is a less prominent feature than in acute infective endocarditis. The vegetations are relatively firm and often greenish in colour; they involve not only the valve cusps but also the mural endocardium and the chordæ tendineæ, which may rupture.

The pathological changes in other organs will vary with the extent and size of the infarcts produced. The spleen is large, and may show infarcts and perisplenitis. The liver may be nutmeg in type from a terminal cardiac failure. The kidneys are the site of small multiple emboli, producing on the surface beneath the capsule minute hæmorrhagic points, which have given rise to the name "flea-bitten kidney." On microscopical examination there is a focal glomerular nephritis. In the brain there may be areas of softening due to emboli.

Differential Diagnosis.—Any patient with evidence of valvular disease who develops pyrexia without obvious cause should be suspected of subacute bacterial endocarditis and repeated blood cultures should be done. If in addition there is evidence of emboli the diagnosis is almost certain. Diagnosis is more difficult if there are no clinical indications of valvular lesions. In such cases the possibility of other causes of continued fever must be considered. These include the enteric group, tuberculosis, deep-seated suppuration, such as perinephric abscess, acute leukæmia, Hodgkin's disease, abortus fever, and glandular fever.

Treatment.—Until the advent of penicillin no treatment was of any avail. This drug should be used in every case in which the infecting organism can be shown to be sensitive to the drug. There is general agreement that the course of treatment must extend over at least twenty-eight days and that the minimum daily dose should be 500,000 units. Double this amount is often recommended. It should be given in equal amounts at three- or four-hourly intervals throughout the twenty-four hours.

With adequate dosage the blood culture becomes negative within a few days, the spleen becomes impalpable and there is a striking clinical improvement. Unless treatment is continued for at least four weeks there is likely to be a relapse. Even when the infection appears to have been completely eradicated a proportion of the patients die with congestive heart failure or as the result of renal damage. This is presumably due to extensive damage during the active infection. The earlier the diagnosis is made and treatment instituted the better the prognosis.

CHRONIC VALVULAR DISEASE

It has already been pointed out that rheumatic endocarditis in most cases leads to chronic valvular deformity. Although acute rheumatism and chorea are by far the most common causes of chronic valvular disease, the condition may perhaps also result from scarlet fever. Syphilis is an important cause of aortic disease appearing in middle life, but this results from syphilitic changes in the aorta spreading to the valve rather than from primary disease in the valve itself.

Before passing to a consideration of the effects produced by lesions of the various valves, it is necessary to lay stress upon the fact that valvular lesions in themselves do not produce any very prominent symptoms; the development of symptoms in valvular disease indicates that the myocardium is

unable to carry on its work efficiently. Such insufficiency results in part from the fact that in the presence of valvular disease the heart is working at a mechanical disadvantage, but in the main it is due to slowly progressive changes in a myocardium previously damaged at the time of the original infection. In other words, cardiac failure in valvular disease is ultimately due to a defective myocardium rather than to valvular damage. Conversely, if the cardiac muscle remains efficient, even severe and multiple valvular lesions may be compatible with normal health.

The mitral valve is affected far more frequently than any other. Indeed, in rheumatic heart disease it is doubtful whether the mitral ever escapes completely, though, obviously, there may be considerable variation in the degree to which it is affected. In a series of ninety-seven autopsies in cases of rheumatic fever collected by Carey Coombs, the mitral valve was diseased in every case, the aortic in fifty-seven, and the tricuspid in thirty-five. Minor degrees of mitral disease may, however, give rise to no definite physical signs, and in practice it is relatively common to detect aortic disease, without mitral involvement, in patients whose valvular disease is undoubtedly rheumatic in origin. Disease of the pulmonary valve is rare except in congenital heart disease. The tricuspid valve alone is never the seat of a chronic endocarditis, but tricuspid disease is fairly frequently associated with rheumatic lesions of the mitral and aortic valves.

If the myocardium is sound, no symptoms may result from a valvular lesion, and often the subjects of chronic valvular disease live out their normal span of life until cut off by some intercurrent disease. Unfortunately, however, this is the exception rather than the rule, and most patients with a chronic valvular lesion ultimately show signs of cardiac failure, which may follow one or more of three main types : congestive cardiac failure, subacute bacterial endocarditis, and in aortic lesions the anginal syndrome, the first being by far the most common.

Mitral Disease

Although mitral disease is usually described under the headings of regurgitation and stenosis, it is very doubtful whether these two processes are not always concurrent, but in the more severe and chronic cases, stenosis is the predominating clinical feature. The diagnosis of pure mitral regurgitation as distinct from stenosis is always a matter of doubt, owing to the frequency of systolic murmurs at the apex, apart from mitral disease.

Mitral disease is so commonly due to rheumatic fever or chorea that the number of persons suffering from mitral disease is an index of the amount of acute rheumatic infection in any given community. Fully developed mitral stenosis is unusual before puberty, and, on the whole, females are more frequently affected than males. The majority of patients are between the ages of fifteen and forty-five, and many fail to survive the latter age.

Morbid Anatomy of Mitral Disease.—At autopsy there is a stenosis of the valve accompanied by more or less incompetence. On naked-eye inspection, the heart in an advanced case of stenosis has a most striking appearance, owing to the great dilatation of the left auricle and of the right side of the heart. The dilatation and hypertrophy of the right ventricle and left auricle might reasonably be expected, as the narrowing of the mitral valve offers obstruction to the flow of blood from the right side of the heart to the left. The left auricle is often enormously dilated and, although hypertrophy of the

muscular wall is not obvious at first sight, comparison of the thickness of the wall with that of a normal auricle shows there is considerable hypertrophy. The dilatation of the right side of the heart is very obvious, and, in consequence, even in the absence of tricuspid disease, this valve is widened and incompetent. Thrombi may be present in the auricles (atria), more particularly in the auricular appendices (auricles); these are usually adherent to the walls, but occasionally a large circular thrombus may lie free in the auricle and act as a ball valve.

The cusps of the mitral ring are thickened and often partially fused as the result of a chronic fibroid infiltration; sometimes there is actual calcification; the chordæ tendineæ are shortened, thickened, and partially fused. Viewed from the auricular side, the mitral valve often shows a funnel-shaped orifice which will not admit the tip of a finger; sometimes the valve resembles a diaphragm separating the ventricle from the auricle, and the opening is reduced to a mere button-hole slit. Recurrences of acute endocarditis often occur on valves already scarred by chronic endocarditis, and in such a case, in addition to the valvular deformities, described above, there may be lines of recent vegetations. From an inspection of mitral valves affected by stenosis it is often obvious that complete closure of the valve is an impossibility. In such cases although stenosis must have been accompanied by regurgitation yet frequently no systolic murmur was present during life.

Physical Signs of Mitral Disease.—The fallacy of assuming that every apical systolic murmur represents an organic mitral incompetence has already been stressed. Mitral incompetence, apart from stenosis, should be diagnosed only in cases with cardiac enlargement, a history of rheumatism or chorea and a harsh blowing systolic murmur best audible at the apex and propagated towards the axilla, such a murmur being often accompanied by a systolic thrill. It may also occur in elderly patients with enlarged hearts and atheromatous changes.

In uncomplicated mitral stenosis there may be little or no enlargement of the heart to the left, as judged by the position of the apex beat or the cardiac dullness. The latter is, however, sometimes increased to the right of the sternum. On palpation a diastolic thrill may often be felt over the apex, and on auscultation in such cases there is a diastolic murmur, often termed presystolic,[1] crescendo in character, which leads up to a markedly accentuated and abrupt first sound. This diastolic murmur is localised, and most commonly situated slightly internal to the apex beat. A systolic murmur may be present in addition, is wider in its distribution, and best heard over the apex and towards the axilla. The murmur of mitral stenosis is usually more obvious if the patient is exercised and then auscultated while lying on the left side.

Often in mitral stenosis no presystolic thrill or murmur is present, but during diastole there is a long rumbling diastolic murmur, best heard at the apex, but without the crescendo character of the presystolic bruit. Such a murmur, often termed mid-diastolic, is commonly heard in patients with mitral stenosis when there is auricular fibrillation.

In mitral stenosis, whether there is a presystolic or a more prolonged

[1] The terms "presystolic" and "late diastolic" refer to the fraction of diastole that immediately precedes the commencement of the first sound, *i.e.*, the beginning of ventricular systole, and are more or less synonymous. The term "auriculo-systolic" is also sometimes used in a similar sense in that auricular systole normally occurs immediately before the commencement of the first sound.

diastolic murmur, the second sound at the pulmonary area is accentuated or sometimes reduplicated, presumably owing to an increased pressure in the pulmonary artery.

The murmurs in mitral stenosis are somewhat inconstant and may vary in character with change of posture or rate of heart beat. In every case, however, the murmur remains diastolic in time, whether best heard late in diastole (presystolic) or more accentuated during mid-diastole. With rapid heart action the murmur extends through the whole of diastole. When auricular fibrillation supervenes, the murmur loses its crescendo character or is replaced by a rumbling mid-diastolic murmur. Diastolic murmurs due to mitral stenosis are frequently though not invariably accompanied by a thrill, which is best felt over the apex impulse with the patient on his left side. It is important to remember that simple accentuation of the first sound at the apex does not indicate mitral stenosis, as it may occur in any heart which is beating rapidly and forcibly.

Symptoms of Mitral Stenosis.—No specific symptoms are associated with mitral stenosis unless the heart muscle is failing. Should this occur, the clinical picture, described under the heading of congestive cardiac failure (*vide* p. 414), will be present. Although patients, even with a considerable degree of stenosis, may live for many years with but little impairment of activity, they are usually under-developed, and even in the absence of failure may show a characteristic malar flush. In congestive failure due to mitral stenosis, hæmoptysis is common. Most often it is due to a pulmonary infarct or to pulmonary congestion and failure, but it may also sometimes occur without evidence of failure.

Prognosis.—The ultimate outlook is always bad in cases of developed mitral stenosis, as the fibroid change in the valve usually progresses steadily, even if slowly. If the patient succeeds in surviving to middle life, the degenerative changes in the heart muscle and arteries, which tend to occur after the age of fifty, throw an increased burden on an already damaged heart, and cardiac breakdown is likely to result. More often the cardiac muscle begins to feel the strain at a far earlier age, and in a majority of patients the onset of auricular fibrillation leads to a condition of complete or semi-invalidism. Even so, with adequate care and treatment, life may be maintained for many years.

Aortic Valvular Disease

Whereas chronic disease of the mitral valve is predominantly rheumatic in origin, this is not true of aortic valvular disease, in which syphilis is almost as important a factor as acute rheumatism. In addition, in later life, disease of the aorta and its valve may result from atheromatous and degenerative changes alone or from subacute bacterial endocarditis. As a general rule it may be said that aortic disease, unaccompanied by a mitral lesion and occurring between the ages of forty and sixty, is predominantly syphilitic. Rheumatic disease of the aortic valves, on the other hand, is common in early life, and, in most, is complicated with mitral disease, though this may be slight. Syphilis involving the aorta and the aortic valves is dealt with elsewhere (*vide* p. 431). Very rarely, rupture of an aortic cusp takes place as the result of a blow on the chest or a sudden strain. When this occurs the patient may be conscious of something in his chest having given way, and the signs of aortic regurgitation are found to be present.

Morbid Anatomy.—The cusps of the aortic valve are thickened and less flexible than normal ; fusion between adjacent cusps may occur, and nodular vegetations which may be hard and even calcified, prevent satisfactory closure of the valve. Sometimes the thickening and rigidity lead to narrowing of the lumen. As a result of the leakage of blood through the aortic valve, additional work is thrown upon the left ventricle, which becomes dilated and hypertrophied.

In syphilitic cases the valve may be greatly shortened and almost appear eaten away. There is not the same tendency to generalised fibrosis and calcification so stenosis is never produced.

Physical Signs of Aortic Valvular Disease.—These depend on whether regurgitation or stenosis or both are present.

Aortic Regurgitation.—The physical signs may be striking, The apex beat is unduly forcible and usually well to the left of its normal site. Over the base of the heart and often down both sides of the sternum there is an early diastolic murmur, blowing in character, which often replaces the second sound. The bruit may be very faint and heard only when the chest is examined in a quiet room. In addition there is often a systolic murmur over the base, when it is described as a to-and-fro murmur.

As well as the early diastolic murmur described above, in some cases there is also a presystolic or rumbling mid-diastolic murmur at the apex, which resembles the murmur of mitral stenosis. This is termed an Austin Flint murmur. Its origin is doubtful, but it may be due to a relative stenosis of the mitral valve in comparision with the dilatation of the left ventricle, which has taken place owing to the aortic lesion. There is often considerable difficulty in deciding whether such a murmur is a Flint murmur or an indication of concomitant mitral stenosis. A history of rheumatic fever, enlargement of the heart to the right, and the age of the patient are important. If the aortic disease is syphilitic in origin the mitral valve will not be involved, whereas with a rheumatic aortic lesion the mitral valve is almost invariably the site of concurrent endocarditis, though it may be slight and of no clinical importance.

Apart from the examination of the heart, other signs may point to aortic regurgitation. The most important of these is a quickly rising and rapidly collapsing character in the pulse, which is known as the *Corrigan* or "*water-hammer*" pulse. Visible capillary pulsation occurs, and may be demonstrated most readily by pressing a glass slide upon the mucous membrane of the lip, when alternate flushing and pallor are observed corresponding to each systole and diastole. When aortic regurgitation is severe, marked arterial pulsation is visible in the neck and in all subcutaneous arteries. The systolic pressure is high and the diastolic low, with a resultant high pulse pressure. A record of the pulse pressure is useful for detecting any increase of the aortic incompetence. When this is only slight, so that very little blood regurgitates back into the ventricle, there may be little or no fall in the diastolic pressure, although a diastolic murmur is audible.

Aortic Stenosis.—When the aortic valve obstructs the outflow of blood from the ventricle, the latter hypertrophies, partly in an attempt to overcome the obstruction, and partly as a result of myocardial involvement. A systolic thrill is felt over the aortic area and there is a very loud harsh murmur, blowing in character, best heard over the base and propagated upwards towards the neck. Usually an early diastolic bruit indicates coincident

regurgitation. With advanced aortic stenosis, which is rare, the heart rate may be slow and the pulse slowly rising in character. Aortic stenosis should rarely be diagnosed in the absence of a thrill, but this must be searched for carefully with the patient in the erect position when there is a rough harsh systolic murmur. In rheumatic cases the heart is usually much enlarged.

Symptoms of Aortic Valvular Disease.—Aortic disease of rheumatic origin is latent as regards symptoms more often than any other organic heart lesion. In the syphilitic cases, however, there is nearly always evidence of associated myocardial involvement, usually accompanied by pain (*vide* p. 432). When failure occurs in aortic disease, attacks of vertigo and sudden syncope are common, and anginal pain is more frequent than in mitral disease. Troublesome throbbing in the neck and headache also occur, which may interfere with sleep. In the later stages of failure due to non-rheumatic aortic regurgitation, mental symptoms such as delusions and hallucinations are often present.

Prognosis.—The bad prognosis which in the past was usually given in aortic regurgitation, was the result of a failure to differentiate between the aortic lesions due to rheumatism and those occurring as sequelæ of syphilis and atheroma. In the rheumatic type the outlook is relatively good, and in the absence of severe carditis or further recurrent attacks of rheumatic fever the patient may live in fairly good health for twenty or even for forty years. In syphilitic aortic disease the outlook is much more serious. If the diagnosis is made early, treatment with arsenicals may be of value (*vide* p. 435), but if the patient has already signs of congestive or left ventricular failure, anti-syphilitic treatment may do harm and will never do good, and the average duration of life is less than two years. Sudden death is a grave risk. With aortic incompetence due to bacterial endocarditis or atherosclerosis the outlook depends more on the general condition of the patient than on the local disease of the heart.

Chronic Valvular Disease of Tricuspid and Pulmonary Valves

Except in congenital heart disease and bacterial endocarditis, the pulmonary valve is rarely affected. In severe mitral stenosis with right-sided dilatation, there may be regurgitation through the pulmonary valve as a result of stretching of the valve ring. In such cases an early diastolic murmur, known as a Graham Steell murmur, is heard along the left border of the sternum, and is indistinguishable from that of aortic disease. The diagnosis rests upon the site of the murmur and the absence of other evidence of aortic regurgitation, but in actual practice it is often found that a murmur, thought to be pulmonary in origin, eventually turns out to be aortic. Pulmonary stenosis is discussed elsewhere in its relation to congenital heart disease (*vide* p. 423).

Although less liable to chronic endocarditis than the mitral or aortic, the tricuspid valve is by no means immune. It is, however, excessively rare to find the tricuspid involved apart from disease on the left side of the heart. Incompetence is common in the later stages of congestive failure, but stenosis is less so. The latter gives rise to a diastolic bruit heard near the lower end of the sternum, but care must be taken not to confuse it with a mitral murmur. A pulsating liver is a valuable sign of tricuspid disease.

CHRONIC DISEASE OF THE HEART MUSCLE

(Myocardial Degeneration)

Ætiology.—The following are the main factors responsible for chronic myocardial disease :—

1. Coronary atheroma.
2. Hypertension.
3. Chronic nephritis.
4. Chronic pulmonary disease, *e.g.*, emphysema, bronchiectasis, chronic bronchitis.
5. Rheumatic heart disease.
6. Syphilis.
7. Hypo- and hyper-thyroidism.
8. Hypovitaminosis, especially of the vitamin B group.
9. Anæmia.

Morbid Anatomy.—Myocardial damage may take one of the following forms :—

(*a*) *Cloudy Swelling.*—This is characterised by unusual softness and pallor of the ventricular muscle, which may be pinkish in colour and is friable to the touch. Microscopically the fibres are swollen and granular. Cloudy swelling is common after prolonged pyrexia from any cause. Complete recovery takes place.

(*b*) *Fatty Infiltration.*—By this is meant a pathological increase in the fat normally present in the epicardium, with an extension or ingrowth of it into the underlying muscle, which may even be replaced by fat. Fatty infiltration occurs commonly, though not invariably, in obese persons.

(*c*) *Fatty Degeneration.*—By this is meant the occurrence of fatty globules within the muscle fibres. It occurs particularly in association with any severe anæmia, such as pernicious anæmia, and the leukæmias. It is conspicuous in phosphorus and chloroform poisoning. In chronic lung conditions the right ventricle may be chiefly affected, otherwise the left usually shows the fatty change most markedly. In the anæmias, the distribution of fatty changes is patchy, giving rise to a characteristic " thrush breast " appearance or " tabby-cat " striation in the papillary muscles. Fatty changes usually follow in the wake of disease of the coronary arteries.

(*d*) *Brown Atrophy.*—In chronic wasting diseases, such as carcinoma or tuberculosis, the heart is often rather smaller than normal, and of a brownish tint on section. It may weigh only half the normal. The muscle is not only brown but friable, and the coronary vessels are tortuous.

(*e*) *Fibrosis of the Myocardium.*—By this is meant an overgrowth of connective tissue in the heart walls. It may occur in localised patches or diffusely throughout the organ ; it may be obvious to the naked eye or require special methods for detection. Fibrosis is invariably a sequel to previous damage brought about in various ways : (i) occlusion or narrowing of the coronary arteries and their branches ; (ii) acute inflammation of the endo- or pericardium extending into the heart muscle ; (iii) syphilitic disease ; (iv) tuberculous infection (very rarely). Narrowing or complete occlusion of the coronary vessels may occur near the origin of the main arteries at the aorta, or distally and diffusely in the smaller ramifications. In the former event a large

area of muscle will be infarcted and gradually replaced by fibrous tissue if life continue. With occlusion of numerous small branches there will be multiple regions of fibrosis. The clinical picture depends on the rate of onset of complete and continued occlusion, and on the size of the vessel concerned (*vide* p. 405). Atheromatous changes in the left coronary artery and its branches lead to fibrosis of the left ventricle, at its apex particularly. The muscle wall becomes thin, pale, and stiffened. Thrombotic material is liable to collect in the ventricular cavities over the region affected. The fibrosis and thinning of the heart wall occasionally leads to sudden rupture or aneurysm formation. Rupture is particularly liable to occur after complete occlusion, before the soft infarct has had time to be replaced by fibrous tissue. In rheumatic disease of the endocardium or pericardium the myocardium is always invaded as well. Syphilis of the myocardium occurs in the form of a few large gummata, or many small ones diffusely scattered ; the septa are frequently involved and heart block is common. Ischæmic fibrosis may also follow syphilitic aortitis. It is remarkable how immune the heart muscle appears to be in miliary tuberculosis, though tuberculosis of the myocardium has been described.

Symptomatology.—The clinical manifestations of chronic myocardial degeneration all result from insufficiency of the cardiac muscle. They vary widely, but may be described under three main headings :—

Cardiac Enlargement.—This is nearly always present, but to detect the enlargement special X-ray methods may be necessary. The brown atrophy of senile hearts is the outstanding exception, and angina pectoris often occurs with little or no enlargement of the heart.

Circulatory Failure.—In the early stages a persistently low exercise tolerance may be the only evidence of disease. Slight exertion, such as hurrying on the level or walking up an incline, produces undue respiratory distress or even precordial pain. Later, in the absence of some sudden terminal event, congestive cardiac failure supervenes.

Special Symptoms and Signs.—Any of the arrhythmias, and particularly extrasystoles, may occur. Heart block may be found. Although sensory symptoms are by no means invariable, pain beneath the sternum, or less significantly over the apex, in the epigastrium, or radiating down the inner aspect of one or other arm is extremely common (*vide* p. 406). Dyspepsia and flatulence, headache, attacks of faintness or dizziness, are frequent. The memory often fails, and all grades of mental disorder may be observed. The character of the heart sounds will depend on the condition of the ventricular muscle. In the absence of valvular disease it is not uncommon to find the first and second sounds altered in quality, but there is no characteristic change. Frequently the sounds are feeble and rapid, the so-called " tic-tac " rhythm. Occasionally reduplication of the first and second sound produces the so-called " gallop " rhythm ; this always indicates a grave prognosis and is often found with cardio-renal disease.

The Heart in Myxœdema.—In myxœdema and cretinism, the capacity of the heart to perform work is often diminished. The important characteristics of the myxœdema heart are enlargement, a slow rate, and electrocardiographic changes. The enlargement of the heart involves all chambers and may be of great degree. The most noteworthy feature of the enlargement is that it diminishes when thyroid extract is administered. The cause of the enlargement is not at present clear, but is probably due to dilatation as a

specific result of thyroid deficiency, in that in the absence of thyroid hormone the capacity for work of the heart is diminished. Sometimes there is a pericardial effusion. An associated anæmia may be a contributory factor.

The sluggish cardiac action is revealed by a slow circulation time, small cardiac contractions as shown by fluoroscopic examination, and the presence of distant heart sounds. The chief electrocardiographic changes are a diminished voltage of the P and Q, R, S waves in all leads. The T waves may be low, flat, or inverted. The waves return to normal amplitude as a result of thyroid treatment.

Congestive cardiac failure only occurs in a small percentage of cases with myxœdema heart. This is apparently due to the fact that as the energy requirements of the body in hypothyroid states are so diminished, the sluggish enlarged heart can deal with them adequately. Indeed, when congestive cardiac failure in myxœdematous patients does occur, there is not infrequently an associated arteriosclerosis. In those instances where the failure is essentially a myxœdematous one, the condition is cured by thyroid treatment.

Deficiency of Vitamin B_1.—In diseases due to deficiency of certain members of the vitamin B group, such as occurs in beri-beri, pathological changes can be observed in the heart. This deficiency may occur in heavy beer drinkers. Histologically, hydropic degeneration of the myocardial fibres with a perivascular œdema can be demonstrated. These changes, however, are not of regular occurrence, and may be found in conditions other than beri-beri. Clinically, there is enlargement of the heart, involving particularly the right side, and cardiac failure with congestion frequently follows.

At autopsy, hypertrophy and dilatation of all the chambers are found. Adequate treatment with vitamin B_1 produces beneficial results, with a diminution in the size of the heart. Digitalis therapy has no such effect.

Clinically, this type of myocardial degeneration is usually associated with peripheral neuritis, but in some cases there is only a history of dietary insufficiency of vitamin B-containing foods.

Cases of pellagra frequently show symptoms and signs of cardiovascular damage, and it is probable that this is due to the association of a vitamin B_1 deficiency in this disease.

In human scurvy, changes in the myocardium have been described. It is not clear that vitamin C deficiency is responsible, for there is usually present a multiple vitamin deficiency and the cardiac lesions may be due to the lack of vitamin B_1. Vitamin C is low in rheumatic fever, but its administration has no effect on the clinical course of the condition and does not reduce the incidence of recurrences.

HEART FAILURE

Apart from special cases such as Stokes-Adams attacks in heart block the heart generally fails in one of three main ways : (i) coronary heart disease with angina pectoris or cardiac infarction, (ii) congestive failure or right ventricular failure, or (iii) left ventricular failure, showing itself by paroxysmal dyspnœa, cardiac asthma, or acute pulmonary œdema. It is true that failure of the left ventricle is often followed quickly or more slowly by failure of the right, but the two syndromes can be distinguished and are important both for treatment and prognosis. These three forms will now be discussed. Peripheral circulatory failure is dealt with on page 419.

CORONARY HEART DISEASE

The blood supply of the heart through the coronary arteries has been described elsewhere (*vide* p. 368), but there are two points in which the coronary circulation differs from that in other organs. First the coronary arteries are at any rate in the healthy heart functional end-arteries, *i.e.*, there is relatively little anastomosis between different branches. Secondly, owing to the contraction of the heart muscles during systole, blood flow takes place only during diastole. In consequence, the " head " of pressure in the coronary vessels is less than that in arteries elsewhere. Owing to these two factors partial or complete obstruction of the lumen of coronary arteries and their branches is likely to produce ischæmia of the tissues of the heart.

The coronary arteries, like those in the rest of the body, are prone to develop atheroma. This process affects primarily the intima, beneath which cholesterol is deposited, and eventually atheromatous ulcers are formed. The ultimate effects of coronary atheroma are to narrow the lumen of the vessels, thereby slowing up the blood flow. Moreover the coronaries, even when healthy, have a relatively narrow bore and complete obstruction may occur. In addition atheroma is very liable to lead to deposition of clot, thus hastening a complete occlusion of the affected artery.

Atheroma of coronaries is by far the most common cause of interference with the blood supply to the heart but rarely other causes may produce similar effects. Thus in syphilitic aortitis the mouths of the coronaries may become obstructed, or very rarely large vegetations on the aortic cusps may interfere with the coronary circulation.

Cardiac ischæmia produces important pathological changes in the heart. Atheroma is seldom confined to one coronary artery or a single branch thereof, and the prolonged ischæmia that results produces degenerative and fibrotic changes in the myocardium, which are often most easily visible in the left ventricle near the apex. These changes ultimately so interfere with the efficiency of the myocardium that the reserve power of the heart is seriously diminished. Demands for increased work by the heart in such a case may lead to attacks of cardiac pain known as angina pectoris (*vide* p. 406). If, however, a coronary becomes completely occluded, infarction of the portion of the heart muscle, which is cut off from its blood supply, results. When this occurs, particularly if the occlusion of the artery has been rapid, dramatic symptoms arise, which are usually termed cardiac infarction or coronary occlusion (*vide* p. 408).

It is important to realise that angina and cardiac infarction though strikingly different in their clinical manifestations are both due, at any rate in 95 per cent. of cases, to coronary atheroma. As might be expected, therefore, the same patient may suffer from both these conditions.

While it is clear that the underlying pathological basis of the anginal syndrome and cardiac infarction is ischæmia of the heart muscle, the mechanism by which the symptoms are produced is less well understood. It is probable that when any muscle is deprived in part of its blood supply a sensation of pain develops. Thus in intermittent claudication (*vide* p. 436) there are symptoms which in many features resemble those of angina. Teleologically the symptoms may be explained as an effort to warn the patient to desist from overexertion.

The age incidence of angina and cardiac infarction is similar. Both are uncommon, though by no means unknown, before forty, and over 80 per cent. of cases occur between forty and seventy. Both show a sex incidence of at least four males to one female. There is undoubtedly a big hereditary factor in the development of atheroma, whether coronary or in other vessels. Consequently angina, coronary thrombosis, and cerebrovascular lesions are often encountered in one family.

It is proposed to describe the symptomatology of angina pectoris and cardiac infarction separately.

ANGINA PECTORIS

Symptoms.—The pain or sensation of constriction or oppression which is termed angina pectoris varies enormously in its type, severity, and frequency of occurrence. It is unusual for the medical attendant to see the patient in an attack and the diagnosis, therefore, depends mainly on the history. Moreover in a considerable proportion of patients with angina nothing abnormal can be found by the most careful physical examination and even X-rays and electrocardiograms may be normal. Clearly in these circumstances the importance of an accurate history both from the patient and his relations is all-important.

The most characteristic form of angina is a pain which comes on during exertion—the so-called angina of effort. The amount of exertion required to bring on the pain varies in different patients and in the same patient from time to time. Walking on the level may produce no symptoms, but going uphill, hurrying, or walking against a strong wind may bring on an attack. The sensation varies from a sense of constriction or oppression to a severe pain. It is first felt behind the sternum but may radiate down the left arm along the ulnar border, sometimes down both arms and rarely down the right arm alone. Frequently it radiates into the neck and jaws and less frequently into the epigastrium. Apart from exertion there may be other exciting factors, such as cold, anger, anxiety, dreams, or a heavy meal, particularly if exercise is taken following a meal. In severe cases attacks may occur even when the patient is at rest in bed—so-called decubitus angina. The duration of even the most severe attacks is seldom over 10 minutes and most are much shorter.

The severity and frequency of the attacks are probably related to the degree of ischæmia in the myocardium, but the character of the patient is also important. There is a wide variation in the sensitivity of different people and those who are hypersensitive to pain are likely to suffer most severely, but this does not mean that their prognosis is worse. Fear of impending death (*angor animi*) is often said to be a feature of anginal attacks, but this is felt mainly by nervous subjects, often terrified by the ominous diagnosis of angina.

During an attack the patient stops whatever he is doing and remains motionless. He is usually more comfortable standing up than lying down. Angina of effort usually passes off quickly when the patient rests. There is no noticeable dyspnœa and no tachycardia, but the blood pressure is often somewhat increased in an attack. The heart may be enlarged to the left, particularly if the patient is a hypertensive subject, and the electrocardiogram

may show inversion of the T wave, especially in lead I. *A normal electrocardiogram does not in any way exclude a diagnosis of angina.*

Course and Prognosis.—Very occasionally death occurs in the first attack of angina, but as a rule the prognosis both as regards life and activity is much more favourable than the average layman thinks. Paul White in an extended follow-up estimates the average period of survival as ten years from the first attack. Not infrequently attacks may cease for long periods and cause relatively minor disability, provided the patient is reasonably careful. On the other hand it is quite impossible to predict what may happen in any particular case and some 25 per cent. develop coronary thrombosis. Many, however, live to reasonably old age. Some 15 per cent. develop congestive cardiac failure. When this occurs the attacks of angina cease. Patients with hypertension and angina may die with left ventricular failure, cardiac asthma, congestive failure or cerebral hæmorrhage.

Treatment.—This consists of the immediate treatment of an attack and more general treatment designed to prevent attacks. For the actual attack vasodilator drugs are of the greatest value. Those in common use are tabulated below :—

Nitroglycerine (*trinitrin*).—This is given as a tablet containing $\frac{1}{1\frac{1}{5}0}$ gr. It is rapidly absorbed if placed under the tongue and is usually effective in stopping an anginal attack within one or two minutes. Sometimes two tablets may be required.

Amyl Nitrite.—This is put up in glass capsules containing 2 or 3 minims. The capsule is broken in a handkerchief and the vapour inhaled. It produces almost immediate relief of the angina but may have unpleasant side effects, such as dizziness and sensations of pulsating in the head, which prevent it being taken for an attack developing in public.

Sodium Nitrite.—This is taken by mouth in $\frac{1}{2}$ to 1 gr. doses. It takes five minutes or longer to be absorbed but the vasodilator action persists for an hour or more. The drug is therefore of use as a prophylactic when angina is recurring very frequently.

Erythrol Tetranitrate.—This drug given by mouth in $\frac{1}{4}$ to $\frac{1}{2}$ gr. doses has a vasodilatory effect for several hours, but as it acts slowly it is of more use for prophylaxis than for the treatment of attacks.

Morphia should not be given for attacks of angina as there is a grave risk of addiction. Brandy may relieve the pain but is less effective than the nitrites.

The Prevention of Attacks.—A patient who is having very frequent attacks brought on by minimal stimuli should be put at complete rest in bed, preferably away from business and domestic worries. The duration of bed rest depends on the progress, but often the attacks will cease within a week or two and strictly controlled activity may be allowed. Phenobarbitone or bromide is often helpful during this period. Moderate restriction of diet is also advisable and meals should be small and frequent.

More often, however, it is not necessary to confine the patient to bed but an effort should be made to avoid factors which precipitate attacks, such as exertion, cold, excitement, or anxiety and fatigue. Such measures combined with a restriction of business activity and reassurance often produce a remarkable improvement both as regards the frequency and severity of attacks.

Various drugs have been recommended as effective. Undoubtedly

sedatives such as phenobarbitone and bromide are of value. Theophylline and its compound aminophylline (cardophylin) in doses of $1\frac{1}{2}$ to 3 gr. given by mouth thrice daily for several weeks may help by producing vasodilatation of the coronary arteries.

Various surgical measures have been tried such as dorsal sympathectomy or paravertebral alcohol injections. These procedures may prevent the attacks of pain but they do not have any effect on the underlying condition of the coronaries.

The differential diagnosis of angina is discussed below with that of cardiac infarction.

CARDIAC INFARCTION

(*Coronary Occlusion, Coronary Thrombosis*)

The pathological basis of cardiac infarction has been discussed above. Often a dramatic seizure, sometimes immediately fatal, may be the first indication of coronary disease but in a large proportion of cases anginal attacks have preceded the coronary occlusion.

The symptoms and signs of cardiac infarction, like those of angina, are very variable, dependant mainly on the size of the cardiac infarct and the suddenness with which the occlusion of the coronary vessel takes place. Small infarctions especially when they occur in relatively hyposensitive or aged subjects may cause few striking symptoms and are often attributed to indigestion. In most cases, however, the symptoms and signs are sufficiently severe and typical to enable a diagnosis to be made on clinical grounds alone.

Symptoms and Signs.—*Pain.*—This comes on very rapidly and starts most often when the patient is inactive or even when he is asleep. The pain, like that of angina, is retrosternal and may radiate as does angina. Not infrequently, however, it is felt low down and may be mainly upper abdominal. The pain is severe and soon reaches its maximum. It lasts not minutes as in angina but for hours or even days. At its onset it may be accompanied by nausea or vomiting.

Dyspnoea.—This is by no means invariable but may be severe and the patient may rapidly develop left ventricular failure.

Circulatory Collapse.—The heart rate is often raised and the pulse thin and thready. The blood pressure falls even in persons previously hypertensive. The skin is cyanosed, grey, cold, and sweating.

Arrhythmias.—The heart may be irregular due to the development of auricular fibrillation, paroxysmal tachycardia, extrasystoles, or occasionally heart block.

When the patient is examined shortly after the onset the heart sounds are weak and "tic tac" in character, or there may be a gallop rhythm. Sometimes a systolic murmur is audible at the apex, probably due to dilatation of the heart. After about twenty-four hours necrosis of the infarct produces pyrexia up to about 101° F., with a leucocytosis of 12,000 to 20,000 white cells, mainly neutrophils. If the infarct extends to the pericardium a rub may be audible, usually very transient.

Not infrequently mural thrombi form in one or both ventricles. These may result either from extension of the cardiac infarct to involve the endocardium or may be due to stasis. If thrombus becomes dislodged, as it often

is between the third and fourteenth days of illness, serious embolic phenomena may result, either pulmonary or in the systemic circulation.

Differential Diagnosis.—Obviously from the point of view of treatment it is important to distinguish angina from coronary occlusion, although both result from the same underlying pathological condition. The main distinguishing features are :—

1. The pain in coronary occlusion is usually more severe and always lasts much longer than in angina. Anginal pain is counted in minutes ; that of coronary occlusion in hours or days.

2. Following an attack of angina the patient is not collapsed or prostrated ; with a coronary occlusion, even though the pain may not have been severe, the patient is obviously ill.

3. Coronary occlusion usually occurs when the patient is at rest ; angina during exertion.

4. Anginal pain rapidly responds to nitrites, while that of coronary occlusion is unaffected.

In some cases where frequent anginal attacks are of recent onset they may indicate gross narrowing of a coronary artery with the likelihood of occlusion in the near future : such cases should be confined to bed and treated with care. In other cases where the history is only of frequently recurring attacks of angina the subsequent course of events clinically and electrocardiographically may prove that there has been a coronary occlusion.

More difficult and more important is the differentiation of cardiac pain, whether anginal or thrombotic, from pain originating elsewhere. In coronary occlusion the pain is sometimes referred to the upper abdomen and may closely simulate perforation of a peptic ulcer. Although there may be shock and collapse in either condition, with a perforation there is great tenderness and guarding on palpation, which is not a feature of coronary occlusion. If there is any real doubt an X-ray film of the abdomen will show gas below the diaphragm in the case of a perforation.

Cardiac pain may be confused with that due to cholecystitis and gall-stones. It is indeed not uncommon for a patient to suffer from both conditions, and it is probable that gall-bladder infections tend to aggravate or even produce angina. Occasionally after cholecystectomy anginal attacks may cease.

Cardiac pain has to be distinguished from that which is so prominent a feature in effort syndrome (*vide* p. 425). In the latter condition the patient locates the pain in the left submammary region rather than behind the sternum and there is often precordial tenderness on percussion, which is not a feature of true cardiac pain whether anginal or occlusive. Moreover, there are likely to be other factors, such as age and psychological make-up of the patient, which will help diagnosis. Pain in effort syndrome is more prolonged than an attack of angina, and is often alleged by the patient to be present continuously for long periods. It is not noticeably increased *during* exertion, though it may be aggravated *after* exertion or by emotion or excitement. Symptoms may be brought on by fatigue and overwork as well as by anxiety.

Spasmodic pain in the chest, often precordial, may occur which is relieved by alkalis or the taking of fluids. This is probably associated with spasm of the œsophagus, the cardiac orifice, or even the pylorus. After taking an alkali such as sodium bicarbonate there is eructation and relief. Such

symptoms are often attributed by the layman to " wind round the heart." It is important that they should not be misdiagnosed as angina.

Less frequently there may be difficulty in the differentiation of coronary thrombosis from dissecting aneurysm (*vide* p. 431), but here the question is mainly of academic interest. Acute pericarditis may cause substernal pain, which is aggravated by respiration or movement. Other acute conditions such as a pulmonary embolism or less commonly spontaneous pneumothorax may simulate cardiac pain.

Electrocardiographic Changes.—These are not constant, but may be conclusive. The conspicuous alteration in the electrocardiogram is in the T wave, which is inverted in leads I. or III. The T wave in lead II. may also be inverted in conjunction with an inverted T either in leads I. or III. The T wave in lead III. may be unusually elevated, when in lead I. it is inverted and *vice versa*. Often that portion of the curve immediately succeeding the R or S wave tends to become raised above or depressed below the base line

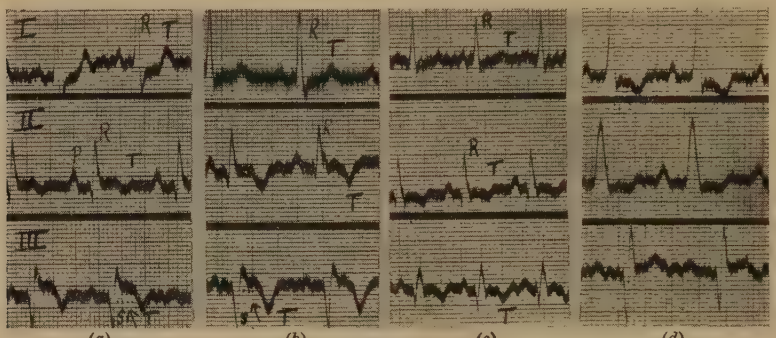

FIG. 22

Electrocardiograms from a man aged 54 (*a*) 5 days, (*b*) 12 days, and (*c*) 14 weeks after a coronary thrombosis, and (*d*) three years later after a second (T I or anterior) coronary thrombosis. In (*a*), in lead III., the portion of the curve during the S T interval is raised above the base line and T is slightly inverted; in (*b*) T is deeply inverted in leads II. and III.; in (*c*) these have returned some way towards the normal. After the thrombosis the temperature rose to 102° for 4 days, the white count rose to 29,000, and the systolic blood pressure fell from 160 to 90 mm. of mercury; in (*d*) three years later, T I has become inverted indicating a second cardiac infarct, this time of the anterior type.

(*From an Electrocardiogram, by Dr Maurice Campbell.*)

(*vide* Fig. 22). Cardiac infarction with T I. inversion indicates infarction of the anterior portion of the heart, generally of the left ventricle. T III. inversion indicates changes in the posterior portion, again generally involving the left ventricle and, other things being equal, is of less serious significance. Sometimes lead IV., which in general features resembles lead I., may show inversion of the T waves before they have developed or after they have disappeared in the other leads.

Course and Prognosis.—Coronary occlusion is the commonest cause of sudden death or of deaths within a few hours or days. When the patient survives the initial period of shock the damage to the myocardium may be such that congestive cardiac failure develops with an ultimately fatal issue. Left ventricular failure is also not uncommon. In a few cases the cardiac infarct softens and the heart ruptures, producing hæmopericardium and sudden death. Even less commonly the scar which replaces the infarcted

area becomes stretched and forms a cardiac aneurysm, which is sometimes visible in an X-ray. In addition to other risks that of embolism is present at least for three weeks.

Unfavourable prognostic features are advanced age, severe pain for over twelve hours, systolic blood pressure below 100, a high leucocytosis or pyrexia lasting over a week, the development of heart block or established fibrillation, and, worst of all, heart failure, whether left ventricular or congestive.

In spite of the many risks attendant on coronary occlusion over 25 per cent. survive for ten years or more and lead active lives. Second attacks are common and carry a higher mortality.

Patients who have survived a coronary occlusion sometimes become strikingly introspective and hypochondriacal, but self-confidence can often be restored by reassurance and tact.

Treatment.—The duration of bed rest will depend on the severity of the case, but every patient diagnosed as coronary thrombosis should be kept in bed for a minimum of a month, and usually six weeks. A further month is spent getting up gradually, and a month of quiet convalescence. There should be no return to work, however sedentary, for a minimum of three months from the onset. Many of the more severe attacks may call for longer periods of treatment.

There is no specific drug treatment, but morphia is essential to control the severe pain : it is best given in $\frac{1}{4}$ gr. doses, frequently repeated as necessary. Papaverine hydrochloride is thought to relieve arterial spasm and so may prevent further thrombosis after a coronary occlusion. It may be given by mouth, 3 gr. repeated up to three times daily, or intravenously, $\frac{1}{4}$ gr. in 1 c.c. saline : if used, papaverine should be given within the first twelve hours. Oxygen may be required for breathlessness or cyanosis, or digitalis if fibrillation develops. Cardiac stimulants such as coramine or strychnine are undesirable. Theophylline ethylene diamine (aminophylline) is sometimes given by mouth in doses of $1\frac{1}{2}$ to 3 gr. four times daily to produce coronary vasodilatation, or it may be given intravenously.

When the patient is fit enough to return to ordinary life this should be so regulated that all strenuous exertion is avoided, but moderate exercise such as walking and golf is both permissible and beneficial. At least eight hours should be spent in bed. Extremes of climate should be avoided.

LEFT VENTRICULAR FAILURE

In all forms of persistent hypertension, whatever its origin, and in aortic incompetence the left ventricle is enlarged partly by dilatation and partly by hypertrophy. Although no symptoms may develop for many years eventually, if life is not cut short by other causes, such as cerebral hæmorrhage, the left ventricle begins to fail. The clinical picture thus produced is known as left ventricular failure.

Sometimes the first symptom is an insidious breathlessness, but not infrequently the first striking manifestations are attacks of severe paroxysmal dyspnœa which occur most commonly at night. Their resemblance to bronchial asthma has led to such attacks being termed *cardiac asthma*. The onset of an attack is sudden ; it often occurs soon after the patient has gone to sleep. He awakes with a distressing sensation of suffocation and is intensely

dyspnœic ; there is, however, generally no anginal pain. He coughs persistently and often brings up large amounts of liquid non-purulent and frothy sputum, which is sometimes pink with blood (acute pulmonary œdema). The attack lasts for about an hour and then suddenly ceases, leaving the patient exhausted. If he is examined during an attack there are innumerable râles all over the chest, particularly at the bases. The pulmonary second sound is often accentuated, indicating that the pressure in the pulmonary circulation is relatively high.

In elderly patients with left ventricular failure mental symptoms may sometimes be prominent. Apart from restlessness and anxiety the patient becomes the victim of terrifying dreams and hallucinations, which may lead to a state of complete confusion and disorientation. If these symptoms develop the patient needs careful watching lest he jump out of bed and injure himself. Occasionally violent delirium develops. As a rule mental symptoms are of grave prognosis.

Attacks of cardiac asthma occur in conditions other than hypertension, though this is the most common cause. Thus they are encountered in syphilitic aortitis and aneurysm, more rarely in rheumatic aortic disease, in coronary heart disease, and rarely in carcinoma of a bronchus.

The mechanism by which an attack of cardiac asthma is produced is relative insufficiency of the left ventricular muscle as compared with that of the right ventricle. This results in an increase of pressure in the pulmonary circulation and ultimately in pulmonary œdema.

Once symptoms of left ventricular failure have developed they tend to persist. Attacks of cardiac asthma become more frequent and may occur almost every night. There is often, though not invariably, a fall in the blood pressure, more marked in the systolic than in the diastolic pressure. As the patient's condition deteriorates symptoms of right-sided failure become apparent with a rise in venous pressure and œdema of the ankles or lumbar region. Eventually the typical picture of congestive cardiac failure may replace that of left ventricular failure.

Treatment of Left Ventricular Failure.—For the immediate treatment of an attack of cardiac asthma $\frac{1}{4}$ gr. of morphia should be given as early as possible. If there is obvious œdema of the lungs with numerous râles and frothy sputum a venesection of 20 oz. often gives relief. Adrenaline and ephedrine may be tried with caution if there is in addition bronchospasm.

When symptoms of left ventricular failure become apparent in a hypertensive subject even though they be relatively slight, it is important to put the patient at complete rest in bed for a month. The rest may give the heart muscle an opportunity to recover and the further development of symptoms may be postponed for months or even years. When pulmonary œdema is present, mercurial diuretics (*vide* p. 418) are of value. In auricular fibrillation digitalis is essential, but even in the absence of fibrillation digitalisation appears to be beneficial in a proportion of cases. Cardiac asthma is less likely to occur if only a very small evening meal is taken and if the patient sleeps well propped up.

CONGESTIVE CARDIAC FAILURE

In congestive cardiac failure, inability of the right ventricle to maintain the circulation efficiently results in typical pathological changes in practically

all the organs of the body ; such changes are the same whatever the cause of the failure, whether associated with valvular disease or due entirely to myocardial disease. The treatment of congestive failure is the same whatever its origin may be.

Morbid Anatomy of Congestive Cardiac Failure.—The pathological changes found at autopsy are best described under the various systems involved.

1. *The Cardiovascular System.*—The pathological changes in the heart are described in the sections allotted to the various types of valvular lesion. In congestive failure, whatever its origin, the right ventricle is dilated, with widening of the tricuspid valve ; the great veins, as a result of increased difficulty in discharging their contents into the auricle, are dilated, and as a result fluid collects in the subcutaneous tissues, particularly those of the most dependent parts. Stasis in the dilated auricles or veins frequently leads to the formation of thrombi, which may become wholly or partially detached and lead to embolism and infarction. Clots from the right auricle will lodge in the lungs, while those from the left side of the heart may produce infarction anywhere in the systemic circulation. Further, as a result of the increased venous pressure, passive effusions may collect in the serous cavities, most commonly in the peritoneum, and less frequently in one or both pleural cavities, and in the pericardium. In severe cases there may be a generalised anasarca, involving, in addition, the abdominal wall and the scrotum.

2. *The Lungs.*—In chronic cases the lungs are tougher and redder than normal, and the condition is described as *red induration*. There may be infarcted areas which result from the occlusion of a branch of the pulmonary artery by an embolus consisting of a detached portion of thrombus formed in the right auricle. Such infarctions are roughly wedge-shaped, and are found with their base on the visceral layer of the pleura ; the infarcted areas are red in colour, and the pleura overlying them shows evidence of a pleurisy, sometimes complicated with an effusion which may be blood-stained. On section of the lung much œdema fluid may be expressed, particularly at the bases. In the bronchi there is an excess of blood-stained secretion.

3. *Alimentary System.*—Owing to the condition of general venous stasis, characteristic changes occur in the liver, and to a less extent in the spleen and alimentary canal. The liver is usually described as *nutmeg* in type, owing to its peculiar appearance on section ; there is considerable general enlargement, and the capsule is tense ; on section, the cut surface consists of a large number of dark red points surrounded by a greyish or yellowish zone ; the red areas are around the central veins of the lobule, while the outer zones of the lobule are yellow from fatty degeneration.

The spleen is firmer than usual owing to increase in its fibrous tissue elements, and in colour a dark purple ; it is rarely enlarged, and sometimes may be smaller than normal. Recent or old infarcts are common.

The mucous membrane of the alimentary canal, particularly in the stomach, is dark and congested.

4. *Kidneys.*—The kidneys in congestive failure are often described as *india-rubber*, owing to the increased toughness of their substance. They are somewhat enlarged, markedly firm, and dark in colour. On section, the cortex is wide and well differentiated from the medulla. Scarring due to old or recent infarcts may be found.

5. *The Central Nervous System.*—Cerebral softening may result from infarction due to clots from the left auricle or fragments of vegetations

detached from the mitral or aortic valves. This may occur in chronic valvular disease, but is more common in subacute bacterial endocarditis.

Signs and Symptoms of Congestive Cardiac Failure.—A patient with severe congestive failure presents so typical a picture that no long description is necessary. Breathlessness is perhaps the most constant and striking feature; even at absolute rest dyspnœa is obvious. When failure of the left ventricle is added the patient breathes far more comfortably while propped up (*orthopnœa*). He is markedly restless and is constantly making attempts to cough, which are often ineffective or may produce a little frothy and sometimes blood-stained sputum. The restlessness and coughing prevent sleep, and in consequence troublesome insomnia adds to the burden thrown upon the heart. The complexion varies from pallor to cyanosis, and the latter is specially marked in the ears, the tip of the nose, and the extremities. Although the subjects of valvular disease are usually thin, this may be masked to some extent by œdema, and the abdomen is distended by ascites and enlargement of the liver. Abdominal discomfort and vomiting are common; the former is due to the enlarged and tender liver, and the latter to the chronic gastritis produced by the passive venous congestion in the gastric mucous membrane. The veins are markedly distended with blood, and those in the neck may be seen pulsating. In the more severe cases profuse sweating may be a striking feature, and the patient is cold and clammy, while the mouth temperature is recorded as subnormal owing to increased breathing through the mouth.

Emboli, consisting either of fragments of clot from the auricles or of portions of valvular vegetations, may produce symptoms depending on the localisation of the infarcts produced. Sudden pain in the chest, with dyspnœa, hæmoptysis, and later a pleural rub, indicate infarction of the lung, which may be followed by a pleural effusion often blood-stained. Emboli from the left side of the heart may produce sudden hemiplegia, due to a cerebral embolus. Pain in the region of the spleen and occasionally a rub may indicate infarction. Other less common sites of embolism are: (i) peripheral vessels in the limbs, especially the legs; (ii) retinal vessels; (iii) mesenteric vessels; (iv) renal arteries, resulting in transient hæmaturia and albuminuria. Embolic manifestations such as those described above occur most frequently in congestive failure and mitral stenosis or in subacute bacterial endocarditis; of the latter condition they may be an outstanding feature.

Such is the clinical picture of severe congestive failure, but sometimes one particular group of symptoms may predominate. Mental symptoms are more common in left ventricular than in congestive failure.

On physical examination, apart from the signs of valvular disease, there may be increased cardiac dullness to the right of the sternum, indicating dilatation of the right side of the heart. On examination of the chest the respirations are frequent and shallow; the percussion note at the bases of the lungs is impaired and, if pleural effusions are present, there may be a board-like dullness; on auscultation râles are heard over the bases, and sometimes signs of a more generalised bronchitis are present. The liver is easily palpable and may extend as low as the umbilicus; it is markedly tender, and may be felt to pulsate. If ascites is present, fluid may be detected by a thrill and movable dullness; often the amount of distension and eversion of the umbilicus may make the diagnosis of ascites obvious without any physical examination.

The pulse is always rapid, and often markedly irregular owing to the

presence of auricular fibrillation (*vide* p. 384). Other arrhythmias, particularly extrasystoles, are frequent accompaniments of congestive failure.

In the milder cases of congestive failure, when the patient has only few symptoms, a careful examination may detect physical signs which point to the true diagnosis. Coarse râles at the bases often occur long before any œdema or marked dyspnœa, and sometimes tenderness under the right costal margin may indicate the early stages of venous congestion of the liver, even though there is no obvious enlargement of that organ. Increased venous pressure may be demonstrated by the failure of the veins of the arms to collapse rapidly when the limb is elevated above the level of the manubrium. Congestive failure, however mild, necessarily implies some degree of breathlessness at rest.

TREATMENT OF CARDIAC FAILURE

The most important factor which determines the onset of cardiac failure is the condition of the heart muscle. If this remains even relatively undamaged the presence of chronic valvular disease will produce few if any symptoms. So great is the reserve power of the healthy myocardium that even moderately severe grades of mitral and aortic valvular disease are not incompatible with reasonable longevity and activity. The presence of chronic valvular disease, however, nearly always indicates that at some time in the past there has been more or less severe inflammation of the myocardium, and this, coupled with the extra strain thrown on the heart muscle by valvular disease, is extremely likely to lead ultimately to cardiac failure. In chronic valvular disease, myocardial insufficiency frequently arises in late middle life as a result of the gradual impairment of the functional capacity of the heart muscle, in common with that of the skeletal muscles.

The Prophylaxis of Cardiac Failure.—The treatment of acute carditis has already been discussed elsewhere, but there remains the problem of the patient who, after an acute carditis, usually due to rheumatic fever, is left with a heart damaged by valvular disease.

1. *Avoidance of Further Attacks of Rheumatic Fever.*—If the patient is a child there is a grave risk that further recurrences of acute rheumatism may cause additional damage to the heart, and it is therefore all-important that the patient should be shielded as far as possible from such attacks. If possible the child should be removed to healthy surroundings in the country, and all factors such as overcrowding and defective nutrition should be eliminated. Unfortunately, under present social conditions this is usually impossible except among the rich. If the patient is of the industrial class, something may be gained by sending him to a special school for rheumatic or invalid children.

2. *Occupation.*—All occupations which involve heavy manual work are highly unsuitable. Clerical or business work of some kind is sometimes a solution. High altitudes and hot climates are to be avoided.

3. *Personal Hygiene.*—Focal infection must be avoided. The teeth should be kept in good order, and all carious or dead teeth removed, as infection from such a source may produce infective endocarditis. Wholesale tonsillectomy in rheumatic patients has nothing to recommend it, but if the tonsils are a focus of chronic sepsis they should be removed. Before any such operation is performed the patient should be given prophylactic penicillin

(*vide* p. 8). When no signs of failure are present an ordinary diet is satisfactory. As regards exercise, though it must be realised that a patient with a damaged heart has a diminished cardiac reserve, it is most important from the point of view of general health that reasonable exercise and fresh air should be encouraged. The patient's own sensations form the best criterion as to the amount of exercise to be allowed. Fatigue and breathlessness will be a sufficient warning that the heart muscle is being overtaxed. Strenuous exercise such as football, boxing, and running must be forbidden, but walking or golf are often beneficial. More sleep is needed by a cardiac patient than by a healthy person, and all factors which produce insomnia must be avoided.

4. *Mental Hygiene.*—It is most important that a patient with a valvular lesion should not be allowed to drift into chronic invalidism through too much concentration on his disability. While it must be explained to him that reasonable precautions must be taken, he should be encouraged to regard himself as capable of a normal and useful life. Not infrequently patients with valvular disease have a haunting fear that they may suddenly drop dead, and it should be explained to them that there is no risk of this occurring.

Treatment of Incipient Failure.—Having dealt with what might be termed the prophylactic treatment of cardiac failure, the case of the patient with a damaged heart who shows early signs of cardiac failure must now be considered. This may be manifested in various ways, such as undue dyspnœa on exertion, tachycardia or arrhythmia, or digestive disturbances. Such symptoms indicate that the capacity of the heart muscle is overtaxed, and are a warning that, in the absence of adequate steps to adjust the life and régime of the patient to his condition, more severe symptoms will develop. As a rule it is desirable that the heart should be rested by confining the patient to bed for a few days, though when the symptoms are slight, prolonged or absolute rest in bed is unnecessary. In cases with threatened failure it is most important to avoid respiratory infections, such as bronchitis, owing to the extra work thrown upon the heart by coughing. Adequate clothing and the avoidance of draughts and damp will contribute to this object, and in times when epidemics of catarrhal disease are prevalent, places where infection is likely to be contracted, such as churches and theatres, should be avoided. An attempt must also be made to minimise unnecessary exertion, such as climbing of stairs. Pregnancy must be avoided at all costs, as it is likely to produce cardiac breakdown. The question of the administration of drugs is a debatable point. Provided the pulse remains regular, it is doubtful whether anything is gained by giving digitalis. If the patient's work involves manual labour he must obtain a more sedentary occupation.

Treatment of Congestive Cardiac Failure

When cardiac failure is established the patient is breathless even at rest, œdema is present, and there may be effusions in the pleural or peritoneal cavities; cyanosis is often marked, and the condition is obviously one in which life itself is in danger. In a large proportion of cases auricular fibrillation is present. The objects of treatment are threefold: the procuring of complete rest, the relief of the venous congestion, and the restoration of a more normal pulse-rate. These points are dealt with in detail on page 417.

1. **Rest.**—Needless to say, absolute rest is essential. Usually dyspnœa prevents the patient lying flat, and a sitting posture in bed is found to be most comfortable. He should be prevented from doing too much for himself, and satisfactory progress depends mainly on careful nursing. Patients with marked orthopnœa are sometimes more comfortable propped up in an arm-chair. The most valuable drug for procuring adequate rest in a patient with severe heart failure is morphia. This should be given in a dose of $\frac{1}{4}$ gr. hypodermically; if there is œdema of the lungs $\frac{1}{100}$ gr. of atropine should be given simultaneously. With such treatment the patient rapidly ceases to be restless and will often obtain a reasonable period of sleep, from which he awakes marvellously improved. No attention need be paid to the theoretical risk of depressing the heart with morphia, and the drug should never be withheld in restless and anxious patients with severe cardiac failure. In milder cases, or after improvement has taken place, chloral, bromide, or paraldehyde may be given by mouth.

2. **Relief of Venous Congestion.**—In severe congestive failure, whatever the lesion, the patient is usually cyanosed, the veins distended, and the heart enlarged to the right. The symptoms may often be relieved, at any rate temporarily, by venesection, and generally this is most useful if done as soon as possible after the patient is seen. From 1 to $1\frac{1}{2}$ pints of blood should be withdrawn. The simplest and cleanest method is, after compressing the upper arm, to insert a needle into a vein at the bend of the elbow and connect it to a suction bottle. With a needle of reasonably wide bore there is usually no difficulty with clotting. The withdrawal of a pint or so of blood at once lessens the strain on the heart and produces an immediate and remarkable improvement. Venesection is of particular value in congestive failure secondary to chronic bronchitis and emphysema. The most dramatic improvement occurs in patients whose red cell count is well over five millions.

3. **Slowing of the Pulse.**—In most cases of severe congestive failure, especially with mitral stenosis, auricular fibrillation is present, and the ventricle is contracting at a rate of 120 a minute, or over. It is important to reduce the heart rate as rapidly as possible, and fortunately in digitalis we have a drug that can effect this object (*vide* p. 386).

There are certain other points that must be considered :—

1. *Diet.*—During the acute stage of failure, owing to the tendency to vomiting, there is no object in attempting to force food upon the patient. A diet of not more than two pints of milk a day, given in small amounts at frequent intervals, is usually satisfactory. The amount of fluids should not be too large, especially when there is much œdema, and the amount of salt in the diet should be reduced to a minimum, though a salt-free diet and strict limitation of fluid intake are unnecessary unless all other measures have failed. When improvement has taken place, meals should still be frequent, small, and dry in character.

2. *Use of Oxygen.*—Oxygen is undoubtedly of value if the patient is cyanosed. It can be given continuously through a nasal catheter after being bubbled through warm water. By moistening the gas excessive drying of the naso-pharynx is prevented, and it also enables the attendant to see at a glance that a steady stream of gas is passing into the catheter. A mask or oxygen tent may be unsatisfactory in cardiac failure if it produces a subjective feeling of suffocation which more than counterbalances the value of the oxygen.

3. *Œdema, Ascites, and Pleural Effusion.*—In all severe cases of congestive failure there is some degree of anasarca. As a rule, under the influence of rest and digitalis this rapidly diminishes, but sometimes the condition is more obstinate. Ascites which seriously embarrasses respiration should be relieved by paracentesis. Pleural effusions are seldom large, but if dullness extend above the angle of the scapula, aspiration often relieves the patient. With the use of mercurial diuretics acupuncture is unnecessary and should never be employed. When anasarca is a prominent feature the administration of Guy's pill is often beneficial. This consists of mercury pill B.P. 1 gr., powdered squill 1 gr., digitalis leaf in powder 1 gr., and extract of hyoscyamus to 4 gr.; one pill may be taken three times a day. As a diuretic, theobromine sodium salicylate is sometimes useful, given for several days in doses of 15 gr. thrice daily.

The most effective treatment for anasarca is the administration of digitalis and the mercurial diuretics, mersalyl (salyrgan), neptal, or esidrone. These last are available in ampoules for intramuscular or intravenous use. A preliminary dose of 1 c.c. of a 10 per cent. solution is given intramuscularly. If this does not produce signs of intolerance, such as hæmaturia or severe diarrhœa, a course of injections at four-day intervals may be started, giving 2 c.c. of the solution. Intramuscular injections are effective or the drug may be given intravenously diluted with 5 c.c. of saline. This is sometimes even more effective, but sudden deaths have been recorded. The diuretic effect is enhanced by giving ammonium chloride by mouth (30 gr. in capsules) two hours before injection. Diuresis occurs mainly during the twelve hours following injection and often 100 oz. of urine or more may be passed in this period. The drug should therefore be given in the morning in order to avoid sleep being disturbed. At the same time fluids are restricted to 40 oz. or less if possible. It is most important *not to give* these drugs if there is evidence of renal failure. The moderate albuminuria, which so often occurs in congestive failure, does not, however, contraindicate its use.

4. *Cardiac Stimulants.*—The multiplicity of drugs to which a tonic action on the heart muscle has been ascribed is sufficient proof that none of them has any specific action. As a general principle it is true to say that repeated hypodermic injections of "cardiac tonics," whether they consist of camphor, strychnine, adrenaline, or other drug, do more harm than good to a patient who is severely ill. Alcohol is sometimes useful not so much from any direct action upon the heart as from its tendency to induce sleep and to allay restlessness and anxiety. It is best given as brandy or champagne.

After-treatment of Cases with Cardiac Failure.—Once a severe cardiac breakdown has occurred the patient will never be fit for any work that involves much physical exertion. It is, however, remarkable what a striking recovery may take place, and patients, even with established auricular fibrillation, may live in comparative comfort for many years. Fibrillation calls for the *continued use of digitalis* in quantities sufficient to keep the heart rate about 70. During convalescence from acute congestive failure, exercise must be begun very gradually; at first passive movements should be started while the patient is still in bed, and these are soon followed by active movements. Great improvement in the exercise tolerance may be gained by a course of progressive remedial exercises under the supervision of an expert in the subject. All the precautions which have been already described above for patients with threatened cardiac failure must be observed, particularly as

regards the avoidance of respiratory infections. When a tendency to œdema persists, mercurial diuretics may be given at three- or four-day intervals indefinitely.

PERIPHERAL CIRCULATORY FAILURE

"Peripheral circulatory failure" is the term used for circulatory disturbance in which there is a diminution in the venous return to the heart, this being due primarily to failure of the peripheral bed to retain its contents, or to loss of peripheral vascular tone resulting in failure of the blood to return to the heart, or finally to an actual diminution in volume of the circulating blood. In congestive heart failure there is a diminution in the venous return secondary to a decrease in the cardiac output with a tendency to engorgement of the veins. In peripheral circulatory failure the veins are relatively depleted.

Peripheral circulatory failure results from many different mechanisms, the chief one being the diminution in volume of circulating blood. The classical clinical picture exhibiting peripheral circulatory failure is that of surgical shock as seen following trauma, hæmorrhage, surgical operation, or perforation of a hollow viscus. The characteristic features are a pale, damp, cold skin, showing a cyanotic tinge, and rapid shallow respiration. The pulse is usually rapid and of very low tension ; the blood pressure is always low ; the pupils are dilated and react sluggishly to light ; the urinary volume is diminished.

It is now generally accepted that the type of circulatory failure which is so commonly seen in conditions of diabetic ketosis, Addison's disease, acute pancreatitis, acute diffuse peritonitis, severe vomiting or diarrhœa, and severe burns is due primarily to peripheral circulatory failure in which there is a diminution in the volume of circulating blood. The clinical appearances in these various conditions are practically identical with the classical picture of surgical shock. Many theories have been put forward to explain the mechanism of peripheral circulatory failure. The chief factors at work in the different conditions are :—

1. A neurogenic reflex causing a peripheral vasodilatation, *e.g.*, as seen in primary surgical shock and a perforated viscus.

2. The diminution in the volume of circulatory blood brought about by one of three mechanisms :

(i) The loss of large quantities of fluid, *e.g.*, in conditions of severe hæmorrhage, vomiting, or diarrhœa.

(ii) The loss of salt where both the sodium and the chloride molecules play an important part, *e.g.*, in diabetic ketosis, Addison's disease.

(iii) The loss or extravasation of plasma, *e.g.*, in diffuse peritonitis and severe burns.

In some cases profuse perspiration and hyperventilation also play a part in diminishing the volume of circulatory blood.

It is important to realise that not infrequently there may be a combination of cardiac (central) failure and peripheral failure. Of chief interest in this connection are coronary thrombosis, pulmonary embolism, and acute infections. For example, in the initial stages of coronary thrombosis it is rare to find signs of congestive cardiac failure, but usual to find the patient in a typical state of shock. Later on, as the state of shock passes off and the

damaged heart has to deal with an increasing volume of blood returning from the periphery, the typical signs of venous engorgement begin to appear, and the picture of congestive cardiac failure develops.

The mechanism of peripheral circulatory failure in myocardial infarction is probably identical with that of the primary surgical shock associated with trauma. Fluid is retained in the relaxed small vessels with a resultant depleted venous return to the heart.

In pulmonary embolism the clinical picture is a variable one, both cardiac and peripheral factors being present in varying proportions. If the embolus is a large one and causes complete obstruction of the pulmonary artery, then death is almost instantaneous and is due to an acute heart failure. In cases where massive embolism is incomplete, death is usually delayed, and in these cases there is a combination of heart failure and shock. When shock is the outstanding factor, the patient is pale and covered with perspiration, and the pulse is almost impalpable ; when the cardiac factor is predominant there is engorgement of the veins of the neck, intense cyanosis, and rapid enlargement of the liver.

In acute infections also both peripheral circulatory failure and cardiac failure may be found. Originally the circulatory collapse in acute infection was attributed to cardiac failure, but it is now generally accepted that apart from rheumatic fever and diphtheria the circulatory failure is usually due to a peripheral mechanism. In those cases where cardiac failure is the predominant feature, it is probable that the heart has already been damaged by arteriosclerosis or other disease prior to the acute infection. Cardiac failure in acute infections is shown by the increase in venous pressure resulting in dyspnœa out of proportion to the fever, and engorgement of the liver. However, the findings are usually complicated by the presence of peripheral circulatory failure, and in this event the clinical picture is similar to that of surgical shock together with the features of the particular infective disease. The skin is pale and sweating, and the cyanosis present has a greyish tinge, being counterbalanced by the pallor. The extremities are cold and there is no dyspnœa. The superficial veins are collapsed and the venous pressure is low. It is probable that the mechanism of the circulatory collapse in the acute infections is also due to a diminution in the volume of the circulating blood, the mechanism of which is not yet fully explained.

Circulatory Failure in Diphtheria.—The cardiac complications of diphtheria are of two main types. In severe cases, towards the end of the first or early in the second week, there may be acute circulatory failure with low blood pressure and a feeble pulse ; gross œdema is not common.

In some cases, especially in those with nerve paralysis, acute diphtheritic myocarditis may occur about the fourth week. Here heart block is not uncommon though the ventricular rate is often relatively fast : vomiting may be a grave warning and dyspnœa, venous engorgement, and a tender liver may follow ; sudden death and left ventricular failure are the serious risks. Peripheral circulatory failure is an added complication in both types.

Though these immediate effects are so serious, the patient ultimately makes a complete recovery if he survives. Except for rare cases of heart block, diphtheria does not produce any form of permanent cardiac damage.

Circulatory Failure in Pneumonia.—It is generally agreed that congestive heart failure is unusual in patients who develop lobar pneumonia with a healthy heart, and the severe dreaded circulatory collapses heralding death

in this disease are due to a peripheral circulatory failure. The pathogenesis of this failure is not clear, but is possibly related to a toxic effect on the capillaries.

Circulatory Collapse in Typhoid Fever.—As in pneumonia, circulatory collapse is usually peripheral in origin, the systemic veins are collapsed, and symptoms and signs of venous engorgement are absent.

In most general infections, except rheumatic fever and diphtheria, the reaction of the heart and circulation is similar to its reaction to pneumonia and typhoid fever.

Treatment of Peripheral Circulatory Failure.—The patient should be kept warm and be given hot drinks, and the foot of the bed should be raised. Saline and glucose solutions may be given by the intravenous, subcutaneous, or rectal routes. Intravenous "drip saline" or intravenous injection of plasma or serum may give dramatic results; strychnine, pituitrin, coramine, adrenaline, and ephedrine are often effective. Continued administration of oxygen is generally useful.

PREGNANCY AND HEART DISEASE

In dealing with this subject there are two generally accepted propositions: firstly, that auricular fibrillation or congestive heart failure should be a complete bar to pregnancy; secondly, that chronic valvular disease without any evidence of failure is compatible with satisfactory pregnancies and labour, provided these are not too numerous nor follow in too rapid succession. The difficult problems in connection with pregnancy and heart disease arise in that class of woman where, with a valvular lesion, there are slight indications that all is not well with the heart muscle, in other words, in cases of threatened cardiac failure. If the doctor is called upon to advise as to whether such a patient should run the risk of pregnancy, the answer should certainly be in the negative. Unfortunately, however, as a rule pregnancy has already occurred before advice is sought, and the problem to be decided between the obstetric surgeon and the physician becomes not whether pregnancy is desirable but how its presence is to be dealt with. The answer will depend largely on the stage of pregnancy that has been reached when the patient is first seen. If she is not beyond the third month, termination of the pregnancy is without danger, but in the later months induction involves probably little less risk than labour at term. On the whole, it may be said that there is a tendency to overrate the danger likely to result from pregnancy, unless the patient has or has had a definite cardiac breakdown. In patients with auricular fibrillation, pregnancy, if allowed to go to term, results in the mother's death in approximately a third of the cases and often in the child's death.

The treatment of pregnant women with damaged hearts is important. During the last few months of pregnancy they should be practically if not completely confined to bed, and under the influence of rest, and perhaps digitalis, the outlook as regards a satisfactory termination is much improved. It is most important that the second stage of labour should not be unduly prolonged, but decision as to the method of delivery must be left to the obstetrician.

The anxiety for a first child and the patient's social circumstances must be

taken into account in deciding whether to advise for or against pregnancy. No woman with organic heart disease, however sound the heart muscle may appear to be, should as a rule be allowed to go through more than three pregnancies ; should there be any persistent diminution in the exercise tolerance following a pregnancy, no further risks should be run. It is not only the risks of labour that have to be considered, but the increased work that children will bring throughout the successive years when the heart is requiring additional rest.

CONGENITAL HEART DISEASE

One of the striking features of congenital heart disease is the apparent absence of any correlation between the physical signs detected on examination of the heart and the severity of the symptoms displayed by the patient. Even with intense cyanosis there may be no murmurs, and little increase in the size of the heart, and, conversely, well-marked physical signs may be accompanied by no apparent disturbance in the circulation and no discomfort. It is to be borne in mind, also, that congenital defects in the structure of the heart are usually multiple, and less often occur singly. A further feature of great clinical interest is the high incidence of subacute bacterial endocarditis in these cases. Even when the anatomical abnormality is so slight that it gives rise to no disturbance in the circulation and throws no extra strain on the myocardium, for example, supernumerary cusps or two cusps in place of the normal three, infective endocarditis with characteristic vegetations is prone to become implanted on the abnormal valve.

Congenital disease of the heart may be defined as a condition in which there are present in the heart and great vessels certain anomalies of structure that have arisen either through arrest of development or possibly through disease occurring during intra-uterine life. Whether such anomalies lead to circulatory disturbances depends on their nature. In many cases the defects are incompatible with life ; in others, the anomaly may give rise to no disturbance of function, being an accidental autopsy finding, such as two or four aortic or pulmonary cusps, patent foramen ovale, or dextrocardia.

Symptoms.—Symptoms of congenital disease of the heart may be present from birth or may develop later. In a large group of cases cyanosis is the first sign and is so characteristic that the terms " blue baby " and congenital heart disease are practically synonymous. It is most marked in the face, ears, hands, feet, and mucous membranes. Among the factors responsible for the cyanosis are : (*a*) a mixture of arterial and venous blood ; (*b*) deficient oxygenation in the lungs ; (*c*) general venous engorgement. There is usually a marked increase in the red cells, up to as many as 11,000,000 ; the specific gravity of the blood is abnormally high and the percentage of hæmoglobin raised. Hæmorrhages from the mucous membranes may occur, and clubbing of the fingers and toes is exceedingly common. Chronic cough and easily induced breathlessness are striking features, and as a rule the child is undergrown, weakly, and succumbs early. Clubbing, cyanosis, cardiac enlargement, and a murmur render congenital heart disease almost a certainty ; the precise nature of the abnormality may be impossible to diagnose. It must be remembered that striking cyanosis may be produced by methæmoglobinæmia or sulphæmoglobinæmia (*vide* p. 282) ; in these patients, however, there is no dyspnœa.

Fallot's Tetralogy.—Where cyanosis is a prominent feature from early in life the commonest congenital abnormality is a mixture of pulmonary stenosis, a ventricular septal defect, an aorta overriding the septum which allows blood from the right ventricle to reach the aorta, and right ventricular hypertrophy. This combination has been known as Fallot's tetralogy, though it might have been called after Peacock, who gave an excellent description of all these points, and who realised its frequency.

The stenosis is sometimes valvular and sometimes rather low and infundibular, and these cannot easily be distinguished, though an absent second sound in the pulmonary area favours the former. The physical signs on auscultation are not very striking, though there is generally a systolic murmur in the pulmonary area and down the left side, and there may be a thrill, either of these being most often maximal in the pulmonary area. In the uncomplicated case the heart is not much enlarged and there is a striking contrast between this and the gross disability which is due to lack of oxygen. The electrocardiogram shows gross right ventricular preponderance.

In addition to increasing breathlessness and cyanosis on exertion or crying, these children often have more severe attacks, provoked by meals or other factors, that lead to unconsciousness. Luckily those who survive most often grow out of these attacks after two or three years of age. Although the colour and the disability do not appear to become progressively worse, in most cases the outlook is very grave and a large number of children die before they are seven, and still more before they are fourteen. A few cases survive to adult life and are sometimes able to lead a reasonable though limited life. Their polycythæmia, which increases the appearance of cyanosis, is of course an essential in getting on as well as this.

Recently, Blalock and Taussig have introduced an operation which by an anastomosis between the subclavian and pulmonary artery carries more blood to the lungs for oxygenation and greatly alleviates the symptoms.

Congenital Pulmonary Stenosis.—With advanced grades of this condition clubbing and cyanosis are striking features ; the precordium is often bulging, and the cardiac impulse heaving and diffuse. A systolic thrill and murmur are present over the pulmonary area, the second sound being feeble or absent. Where pulmonary stenosis occurs without other congenital abnormalities, the cyanosis may be relatively late in developing, and polycythæmia and clubbing of the fingers are generally less than in Fallot's tetralogy.

Patent Interventricular Septum.—A harsh systolic murmur may be heard to the left of the midline in the third and fourth spaces, sometimes accompanied by a thrill. This is the commonest cardiac defect to give rise to physical signs and accounts for a good number of the cases found in children at routine medical examinations. Fortunately it is generally a small opening that does not give rise to clinical symptoms and has an excellent prognosis.

In other cases the defect is combined with pulmonary stenosis.

Defects of the Interauricular Septum.—Patent foramen ovale is the commonest variety of congenital heart disease found post-mortem. In most cases, however, the opening is not large enough to produce symptoms (though it may produce a systolic murmur) except that it may enable an embolus which originated in a peripheral vein to reach a systemic artery with the production of so-called " paradoxical embolism."

Auricular septal defect in which the opening is large and of different embryological origin has been distinguished. It is most often diagnosed

between twenty and fifty years of age, and a most striking feature is a much better capacity for effort than might be expected on the size of the heart, with cyanosis on exertion only or developing late in life (*cyanose tardive*).

The apex beat is forcible and displaced to the left, and there is generally a systolic murmur both in the mitral and pulmonary areas with some accentuation of the second sound. Clubbing of the fingers is not striking but may be present in about one quarter of the cases. Cyanosis from birth is rare, not being found in more than one case in twenty of those diagnosed as adults. On X-ray examination there is general enlargement of the heart, chiefly to the left, though the right auricle may show to the right. The pulmonary artery is always very prominent and often its branches also, and there may be striking pulsation, though only a proportion of the cases show the " hilar dance." The electrocardiogram shows right ventricular preponderance. The combination of this with mitral stenosis is by no means uncommon, and it is the only congenital disease in which fibrillation is common.

Patent Ductus Arteriosus may be found alone or in combination with other lesions. It is a short thick trunk connecting the pulmonary artery (left branch) and the aorta. It is sometimes associated with pulmonary stenosis, transposition of the great vessels, or stenosis of the aorta. Cyanosis and clubbing are absent in this condition and the diagnosis depends almost entirely on the presence of a harsh murmur of maximum intensity in the second left interspace. The murmur persists usually throughout systole and diastole, with systolic accentuation. It is transmitted upwards and to the left, and may be well heard in the left interscapular region. It is commonly accompanied by a thrill and sometimes by a " water-hammer " pulse. In the last few years many of these cases have been cured by the operation of tying the patent ductus. In skilled hands the risk is not great, but it increases after the patient has passed fourteen to eighteen years of age. Even cases where infective endocarditis has developed have been cured in this way.

Dextrocardia.—The heart is on the right side as the result of transposition of the viscera, the stomach and spleen being on the right and the liver on the left side. Very rarely the heart is alone transposed. Dextrocardia has no clinical significance, but must be distinguished from a heart displaced to the right by intrathoracic disease. As it is inherited as a Mendelian recessive character it is more common in the offsprings of first cousin marriages.

Coarctation of the Aorta.—This produces a characteristic clinical picture and is not very rare. There is some stenosis of the aorta, varying from simple narrowing to complete obstruction, near the insertion of the ductus arteriosus and below the origin of the left subclavian artery. This results in a high blood pressure in the head and arms and a feeble or absent pulse in the abdominal aorta and femoral arteries. In spite of the poor pulse in the legs with a low blood pressure the circulation of the lower part of the body is well maintained by the development of a collateral circulation, by arteries round the scapulæ, by the internal mammary and epigastric arteries, and by the intercostal arteries. These last cause the notching of the ribs that can be seen on X-ray examination. The condition will be diagnosed more often if the femoral pulse is felt for in all obscure cases with undue pulsation in the neck, basal systolic murmurs, or unexplained high blood pressure.

In spite of the high blood pressure, which generally rises no further after adolescence, the heart may not be much enlarged unless there is also aortic incompetence. This may follow congenital bicuspid aortic valves which are

not uncommon ; congenital cerebral aneurysms may also be associated and may be a cause of death.

In cases which remain free from symptoms till adult life the prognosis is relatively good. Where it produces symptoms earlier many do not live beyond thirty years of age. Recently Crafoord of Sweden has successfully operated on some of these cases, doing an end to end anastomosis of the aorta after removal of the constricted portion.

EFFORT SYNDROME

(*D.A.H., Da Costa's Syndrome, Neuro-circulatory Asthenia*)

During the war of 1914-18 large numbers of soldiers were off duty with a diagnosis of " Disorderly Action of the Heart " (D.A.H.) in contradistinction to " Valvular Disease of the Heart " (V.D.H.). Their main complaints of breathlessness, precordial pain, and palpitation were unaccompanied by objective evidence of heart disease. In the present war, though similar cases have occurred they have been relatively infrequent. Similar symptoms had been noted in the American Civil War, and less commonly in peace time.

Clinical Picture.—The most frequent symptoms of which these patients complain are fatigue, palpitation, dizziness, breathlessness even on slight exertion, left submammary pain, nervousness, and sweating. On physical examination the pulse even at rest is relatively rapid, often over 100, respiration tends to be rapid, and the patient is often obviously nervous, tremulous, and excitable. Visible sweating of the palms and axillæ are often striking features even in cold weather.

Inquiry into the patient's history usually elicits that he has always been regarded as delicate and often has been stopped from playing games at school. General physique and muscular development are usually under average, and the patient often gives a history of a tendency to hypochondriasis and nervous instability. Though similar symptoms may have been present in lesser degree in ordinary life they become markedly accentuated on joining the fighting services. In about half the cases there is a family history of neurosis.

On physical and radiological examination there is no evidence of cardiac enlargement nor of any organic disease of the heart. The sleeping pulse-rate is lower or normal. On percussion of the chest wall in the left submammary region the patient may complain of tenderness. The blood pressure is usually normal or over average. Occasionally systolic murmurs may be audible but these are not suggestive of valvular disease (*vide* p. 372). Electrocardiograms show no evidence of myocardial lesions.

Ætiology.—Effort syndrome is seldom seen among members of aircrew, in the Navy, or those branches of the Services for which men volunteer. This is due in the main to careful selection, both executive and medical. The type of serving personnel who during the war of 1914-18 developed gross hysterical manifestations or D.A.H. have during the recent war tended to develop obscure abdominal symptoms, anxiety neuroses, depressive states, and amnesia.

The great majority of patients with symptoms of effort syndrome are aiming at escaping from unpleasant Service duties, and though they are not often malingerers they are anxious to exaggerate their symptoms in the hope that a supposedly diseased heart will give them an honourable escape to civil

life. Unfortunately, frequent reference to specialists, hospitalisation, and investigations, such as electrocardiograms and X-rays, tend to perpetuate rather than relieve their symptoms.

Occasionally similar symptoms may occur after febrile illnesses such as influenza. Only too often these are diagnosed as myocarditis and rest is unwisely advocated, which tends to perpetuate the symptoms.

Differential Diagnosis.—The more these patients are examined and investigated the less the prospect of cure. The whole picture is so characteristic that a cursory physical examination is usually sufficient to exclude organic heart disease, thyrotoxicosis, and pulmonary tuberculosis; this last, however, must be remembered, and it is always prudent to have an X-ray of the chest. The whole attitude of the patient with effort syndrome is completely different from that seen in organic heart disease.

Treatment.—A good regimental medical officer will often be able by tactful reassurance, encouragement, and simple psychotherapy to ameliorate if not cure the milder cases. It is doubtful if more elaborate psychotherapy is likely to be effective. A diagnosis of effort syndrome, or, worse still, any of its synonyms, should never be made, and it is better that they should be labelled as anxiety neurosis, which does not cast aspersions on the heart. Some improvement may be obtained by graduated exercises in an atmosphere of expectation of cure, though many will fail to respond. Many of the patients can be rendered fit enough to carry on in lower grades, where their employment calls for less physical and mental stamina, but there will necessarily be a considerable residue completely useless for any form of Service life. These should be invalided as psychiatric cases and not under diagnoses such as effort syndrome.

HYPERTENSION AND ARTERIOSCLEROSIS

Considerable confusion has arisen in connection with arterial disease and hypertension owing to the multiplicity of terms that have been employed in describing the pathological and clinical conditions involved. From the purely pathological point of view three varieties of arterial change may be recognised: (i) arteriosclerosis, (ii) arteriolosclerosis, and (iii) Mönckeberg's sclerosis. Often all three of these may coexist in a single patient, but more frequently there is a preponderance of one type of change which may have an important bearing on the symptoms presented.

Arteriosclerosis.—This condition, often described as atheroma, may involve both the large arteries, especially the aorta, and the smaller vessels. The arteriosclerotic changes are specially striking in the descending thoracic and abdominal aorta. The coronary arteries are very frequently involved, as are also the main branches of the aorta and the cerebral arteries. The condition primarily affects the intima, the early atheromatous lesions appearing as slightly elevated yellow streaks. These areas later become necrotic, and atheromatous ulcers form which frequently become calcified.

The result of widespread atheromatous change in a large artery, such as the aorta, is a great diminution in its elasticity, which is sometimes associated with some dilatation of its lumen. Aneurysms due to arteriosclerotic changes occasionally arise in the carotid, but in the aorta they are almost invariably due to syphilitic aortitis (*vide* p. 431), and atheromatous changes produce no

more than a general dilatation of the aorta. Sometimes atheroma may spread down to involve the aortic cusps, thus rendering the valve incompetent. In the smaller arteries, such as the coronaries, proliferation of the intima and the formation of atheromatous plaques may so much reduce the lumen that eventually it may become completely occluded by formation of thrombus.

Arteriolosclerosis.—In contrast to arteriosclerosis, where even in the smaller arteries the changes are visible to the naked eye, in arteriolosclerosis the changes involve only the arterioles, and are visible only on microscopical examination. This pathological process occurs most frequently and most strikingly in the kidneys, and for a description of the histological appearances reference may be made to page 510 where the nephroscleroses are described. Apart from the kidneys, similar changes are found in the spleen, pancreas, and liver, but not in the arterioles of the lungs, myocardium, or skeletal muscles.

Although arteriolosclerosis is a purely histological finding, it is of great importance, as it is the earliest and sometimes the only change in the arterial system in essential hypertension.

Mönckeberg's Sclerosis.—This type of arterial disease affects mainly the arteries of the lower limbs of elderly persons. Here the media becomes calcified, often in a series of rings, producing the " pipe-stem " artery, which can often be visualised in an X-ray owing to the presence of calcium. The elasticity of the arterial wall is lost, and as a result the blood supply to distal parts is diminished. This may lead to intermittent claudication or gangrene of the toes.

The Normal Blood Pressure.—Our knowledge of the blood pressure in normal persons has been obtained mainly from the statistics of life insurance examinations. The average pressure in the brachial artery at varying ages shows a gradual increase in both systolic and diastolic levels with advancing age. Wide variations of blood pressure readings are, however, compatible with perfect health. In general it may be said that for adults a systolic blood pressure below 100 mm. of mercury or persistently above 150 mm. is likely to be an indication of disease. Even in the same individual there may be variations of as much as 20 mm. or more from time to time, depending on such factors as posture, excitement, exercise, and meals. On the whole, the diastolic pressure is less liable to variations than the systolic. The normal range of diastolic pressure is from 70 to 95 mm. Diastolic pressures definitely above 100 mm. are always pathological.

The technique of blood-pressure estimations can be learnt only by practical experience, and no attempt will be made here to give in detail the procedure to be adopted with various types of sphygmomanometers. It is, however, important to realise that the first reading may be too high, more particularly if the patient is nervous or excited. With a mercury sphygmomanometer there is little possibility of error in the instrument itself, but dial types of machine readily become inaccurate, and should be repeatedly checked. The cuff must fit evenly round the arm ; a quick reading of the systolic pressure should first be taken by palpation and then a more careful reading by auscultation.

ESSENTIAL HYPERTENSION

Although high blood pressure has long been known to be a concomitant of renal disease and of arteriosclerosis, the recognition of a clinical condition in

which a raised blood pressure is an apparently primary condition is mainly due to the late Sir Stafford Allbutt, who coined the term "hyperpiesia" to describe such cases. Perhaps simpler is the term "essential hypertension."

By no means all persons with high blood pressure can be regarded as suffering from essential hypertension, for it is well recognised that in most patients with renal insufficiency there is some elevation of blood pressure. Also certain rare disorders of the endocrines, such as basophil adenoma of the pituitary (*vide* p. 223) or tumours of the adrenals (*vide* p. 219), may produce high blood pressure. Nevertheless essential hypertension is far more commonly encountered than is high blood pressure due to all other causes put together. Moreover it is difficult, if not impossible, to draw clear lines of distinction between essential hypertension and arteriosclerosis, for essential hypertension sooner or later is always accompanied by a varying degree of arteriosclerosis, and many of the symptoms attributed to hypertension are really the result of ischæmia, due to localised arteriosclerotic changes. It probably is not an exaggeration to say that most cerebral vascular disease, the greater part of chronic heart disease, and a not inconsiderable proportion of renal disease are the ultimate results of essential hypertension.

Pathology.—The most prominent post-mortem findings are cardiac hypertrophy, mainly of the left ventricle, and arteriolosclerotic kidneys. The naked eye and histological appearances of the latter are fully described on page 510. In addition there will be a varying degree of arteriosclerotic change depending on various factors such as the age and the duration of hypertension.

Ætiology.—Although hypertension and its sequelæ probably account for a quarter of all deaths which occur after fifty years of age, there is still uncertainty as to the underlying causes of the condition. Many theories have been put forward, most of them with little or no experimental or clinical evidence for their support. Thus it has been maintained that the hypertension is due to pressor substances in the blood, to disturbances of the endocrines, particularly the adrenals and pituitary, and to disorders of protein metabolism.

Although almost from its name essential hypertension was thought to be independent of renal disease, in recent years Goldblatt has succeeded in producing chronic hypertension in animals by constricting the renal arteries. The diminution in renal blood flow so produced renders the kidneys relatively ischæmic, and the ischæmic kidneys produce a pressor substance, which, when it passes into the circulation, gives rise to hypertension (*vide* p. 508). Possibly, therefore, in the essential hypertension of man the primary change may be an ischæmia of the kidneys due to an antecedent sclerosis of the renal arterioles (renal arteriolosclerosis).

The one outstanding feature of essential hypertension is that at any rate in a very high proportion of cases there appears to be an inherited and constitutional basis. That hypertension and its sequelæ, such as cerebral hæmorrhage and cardiac disease, "run in families" is proved up to the hilt not only by statistics but by the personal experience of every medical practitioner.

It is extremely difficult to estimate the importance of environmental factors, such as the increasing stress of everyday life, tobacco, and alcohol. Although it is true that in the last half-century there appears to have been an increase in arterial disease and its sequelæ, this may be partly due to increasing longevity of the population and more accurate diagnosis. Thus it must seem

remarkable to the student of to-day that the clinical features of coronary occlusion were not recognised until 1924. Nevertheless it seems probable that prolonged and excessive indulgence in food, drink, and tobacco may have an adverse effect on the arterial system.

Symptoms.—As it is impossible to assess with any accuracy the degree to which hypertension is associated with arteriosclerotic changes in any individual case, it is difficult to determine what symptoms are to be attributed purely to hypertension. High pressures such as 200 mm. systolic and 130 diastolic are often found in apparently healthy persons. It is indeed doubtful whether a high blood pressure *per se* produces any symptoms. When these occur in a patient with essential hypertension they are due not so much to the raised pressure as to the secondary changes in the heart and other organs resulting from diminution in the blood supply.

The manifestations, therefore, which may be ascribed to hypertension and its sequelæ are very varied and need not be dealt with in detail, as their clinical features are described elsewhere. The more important, apart from malignant hypertension (*vide* p. 430), are tabulated as follows :—

1. *Cardiovascular System.*
   - (*a*) Coronary sclerosis—angina (*vide* p. 406).
     Coronary occlusion (*vide* p. 408).
   - (*b*) Left ventricular failure—attacks of cardiac asthma (*vide* p. 411).
   - (*c*) Congestive cardiac failure (*vide* p. 412).
   - (*d*) Arrhythmias, especially extrasystoles ; also auricular fibrillation and heart block.
   - (*e*) Aortic regurgitation due to atheroma of valve cusps.
   - (*f*) Intermittent claudication and gangrene.
2. *Nervous System.*
   - (*a*) Headaches (probably due to cerebral arteriosclerosis).
   - (*b*) Vertigo and tinnitus.
   - (*c*) Cerebral hæmorrhage and thrombosis.
   - (*d*) Mental symptoms (*vide* p. 763).
   - (*e*) Hypertensive encephalopathy (*vide* p. 593).
3. *Eye.*
   - (*a*) Retinal arteriosclerosis.
   - (*b*) Papillœdema.
4. *Renal System.*
   - (*a*) Albuminuria and casts.
   - (*b*) Impaired renal function (unusual).
   - (*c*) Uræmia (rare).

Most of the conditions tabulated above need no further discussion in this connection, as they are dealt with elsewhere.

Retinal Changes with High Blood Pressure.—Owing to arteriosclerotic changes the arteries appear narrower than usual, are tortuous, and reflect a bright line of light along their course, the so-called " silver wire " appearance ; also where they cross the veins the latter appear to be constricted. Retinal hæmorrhages are common, and there are often white areas which vary very much in size and number. The degree of impairment of vision depends mainly on the location of the lesions. Hypertensive neuro-retinopathy as

seen in malignant hypertension and chronic glomerulo-nephritis is described on page 509.

Treatment and Prognosis of Hypertension.—As we have no certain knowledge regarding the ætiology of essential hypertension and arteriosclerosis, nor of the mechanism by which they are produced, it can be understood that the situation as regards treatment is unsatisfactory. At the best it can be but palliative.

Attention must be paid to the general regime. Focal infection should be dealt with, especially in hyperpiesia. Most of the patients will be found to be leading too strenuous a life, especially as regards mental activity. Although it is not usually necessary to advise a complete cessation of business activities, the hours of work must be curtailed, and, above all, mental fatigue and anxiety must be avoided. Physical strain is liable to produce serious symptoms, but reasonable exercise is beneficial; the amount of exercise advisable is best regulated by the patient's own sensations.

Great stress has been laid on the diet in high blood pressure. If the patient is overweight there is often benefit from a general limitation of the diet, which produces a loss of weight. On the other hand, it is unnecessary and often harmful to render life a misery by too strict a dietetic regime. Meat should be much curtailed but not omitted; plenty of fresh vegetables and fruit are advisable, as these tend to combat constipation; liquid paraffin is also useful from this point of view. The use of alcohol and tobacco should be limited, but here again it is unnecessary to render the patient unhappy by a complete veto, which in any case is likely to be disregarded.

While it is necessary to emphasise to the patient the importance of adhering to general instructions as to regime and diet, it is important to prevent a continual concentration of his mind on his blood pressure. The use of the sphygmomanometer should be restricted, as too frequent estimations lead only to anxiety and give no helpful information. It is always unwise to allow the patient to know the exact blood-pressure readings.

No drugs have much permanent effect in reducing a high blood pressure. Nitrites reduce the blood pressure temporarily, but are only useful in allaying urgent symptoms such as cardiac pain. Potassium thiocyanate has been used, but toxic effects are frequent and sometimes dangerous. Bromides or luminal may help the patient to sleep and to attain that attitude of philosophic calm which should be the object of treatment. In the plethoric type of patient the removal of 20 oz. of blood by venesection often produces an improvement, and may be repeated at intervals.

The outlook as regards life is very variable, and all patients with a blood pressure of over 200 are precarious lives. A fall in the systolic pressure is often an unfavourable sign, as it may indicate the onset of cardiac failure. Death may occur at any time as the result of cerebral complications or of cardiac failure. On the other hand, life is often prolonged for many years even with pressures of over 200, so that it is justifiable to give a reasonably good prognosis to the patient himself, though the relatives should be warned of the dangers attendant on the condition.

Malignant Hypertension.—Whereas in the great majority of instances of essential hypertension death occurs from sequelæ involving the heart or brain, in a small proportion, probably less than 5 per cent., the renal arteriolosclerosis is accompanied by necrosis and endarteritis of the renal arterioles. This occurs most often in patients under fifty years of age and sometimes even in

relatively early adult life. The diastolic pressure is much elevated, rarely below 130. The clinical picture of malignant hypertension is completely different from that of other forms of hypertension. The most prominent symptoms are those due to increased intracranial pressure, consisting of very severe and intractable headache, nausea, and vomiting, and sometimes epileptiform convulsions and other nervous symptoms as described under the heading of Hypertensive Encephalopathy (*vide* p. 593). On examination papillœdema is invariably present, and the C.S.F. pressure is raised to 250 to 350 mm. of water. The clinical picture may simulate a cerebral tumour. In addition to the symptoms due to increased intracranial pressure, there is a progressive deterioration of renal function. Albumin and red cells are found in the urine in varying amounts, and the blood urea ultimately rises. The specific gravity tends to become fixed at about 1010. The renal aspects of malignant hypertension are discussed on page 508. In the later stages there is often a tendency to hæmorrhage, including epistaxis and purpura.

The outlook in malignant hypertension is extremely bad. Death usually occurs within two years of diagnosis and often earlier. In those cases where renal function is unimpaired bilateral dorsal sympathectomy has given promising results.

Dissecting Aneurysm of the Aorta

In this relatively rare type of aneurysm there is a rupture through the intima so that blood is effused into the media, the layers of which become split. In most cases the tear into the media is situated in the arch of the aorta and the effused blood tracks through the media both towards the aortic valves and down the descending aorta. The dissection may involve the carotids and subclavian, and often extends downwards into the abdominal aorta. The condition most often occurs in males of middle age and over who suffer from high blood pressure. Sudden exertion, such as lifting a heavy weight, appears to be a precipitating cause. Syphilis is not a factor.

The chief symptom is sudden and very severe pain, most often substernal, but sometimes high in the epigastrium ; in addition there is often vomiting and collapse, and not infrequently the condition may simulate a severe coronary occlusion or even a perforated peptic ulcer. The dissection may spread up the carotid and lead to cerebral symptoms. Narrowing of the lumen of arteries may cause the disappearance of arterial pulsation in the limbs, most often in one or both legs. Owing to the loss of blood supply the legs may become cold or even appear to be paralysed.

In about 80 per cent. of cases the condition proves fatal within a few days, and sometimes it may be the cause of sudden death. Often the effused blood bursts through into the pericardium or pleural cavity.

No treatment is available except morphia and complete rest.

SYPHILIS OF THE AORTA AND AORTIC ANEURYSM

Aneurysms of the thoracic aorta are almost invariably syphilitic, as is valvular disease beginning in middle life and confined to the aortic valves. Even during the secondary stage of syphilis changes are already in progress in the arteries, more especially in the aorta and cerebral vessels.

Ætiology.—Though syphilitic aortitis and aneurysm of the aorta occur occasionally in females, the majority of cases are males between the ages of forty-five and sixty. As a rule, a latent period of approximately twenty years elapses between the primary infection and the development of symptoms referable to aortic disease.

Pathology.—The part of the vessel most frequently affected by syphilis is the ascending portion and the arch; less commonly the descending thoracic aorta is involved, and syphilitic disease of the abdominal aorta is extremely rare.

In syphilitic aortitis, the primary pathological change consists in involvement of the minute vessels which supply blood to the arterial wall; these are known as the *vasa vasorum*. Surrounding these are found collections of lymphoid and plasma cells, which are sometimes necrotic and resemble gummatous nodules seen elsewhere. The lumen of the vessels is often diminished or obliterated owing to the proliferation of the intima. As a result the blood supply to the wall of the aorta is deficient, and the more highly specialised tissues—the muscle and elastic fibres—degenerate and are replaced by fibrous tissue. On microscopical examination the media is found to contain irregular strands of fibrous tissue, and the circular elastic fibres are fragmented. Possibly as a compensatory change due to weakening of the media, the intima is thickened and fibrous. On naked-eye examination the interior of the aorta appears wrinkled with fine longitudinal rugæ, irregular folds, and small nodular swellings. Unlike atheroma, syphilis does not produce ulceration or calcification of the intima, though atheromatous changes may also be present.

Similar changes may occur in the aortic valves and cause scarring and thickening which render them incompetent. When the process involves the orifices of the coronaries it may lead to narrowing at the point of entry, though the syphilitic process rarely extends beyond the mouth of the coronary vessels.

As a result of syphilitic aortitis, the vessel loses its elasticity, and the strength of the coats of the artery is diminished. The fibrous tissue which largely replaces the muscular and elastic fibres becomes stretched as the result of the continued arterial pressure, and dilatation may occur with the formation of a saccular or fusiform aneurysm. The *Spirochæta pallida* has been demonstrated in the walls of the vessel.

Symptoms of Syphilitic Aortitis.—In its earlier stages syphilitic aortitis is usually symptomless, and is often only discovered at autopsy. In the absence of complications, such as aortic regurgitation and aneurysm, the most frequent symptom is a sense of substernal oppression; sometimes this may be little more than a feeling of discomfort, but it sometimes amounts to pain, which is comparable with that of angina pectoris. In fact, in syphilitic aortitis the anginal syndrome (*vide* p. 406) is not uncommon. The pain and feelings of oppression often occur after exertion or excitement, but when the condition is well established the attacks may take place at any time. In addition attacks of cardiac asthma may occur (*vide* p. 411).

Physical examination is often negative, but a systolic murmur is occasionally heard. The diagnosis rests mainly upon the symptoms, a positive Wassermann reaction, with or without a history of syphilis, and sometimes a characteristic X-ray appearance of the aorta. If aortic regurgitation is present, the physical signs associated with that lesion will be detectable.

It is impossible to lay too much stress on the importance of considering the possibility of syphilis in every non-rheumatic patient over forty years of age who develops aortic valvular disease or symptoms which might be referable to the aorta. Needless to say, if treatment is to be effective it must be begun as early as possible, before irreparable damage has occurred, such as disease of the valves or aneurysm.

Aortic Aneurysm

Aortic aneurysm is but an advanced stage of syphilitic aortitis. Although almost invariably syphilitic, probably other factors are involved in addition. The disease is at least ten times more common in men than in women, and this is due to heavier muscular work and an increased incidence of syphilis. At least 90 per cent. of patients suffering from aneurysm of the aorta give a positive Wassermann reaction in the blood.

Aneurysms of the aorta have been classified into three pathological types ; saccular, fusiform, and dissecting. Saccular aneurysm is due to a localised weakness in the aortic wall ; the fibrous tissue gradually stretches until a sac is formed, which may ultimately become larger than a tennis ball ; it communicates with the lumen of the aorta by an opening which may be comparatively small. In the fusiform type of aneurysm there is a general dilatation of the vessel, which may involve the ascending aorta and the arch. Dissecting aneurysm is described elsewhere (*vide* p. 431).

The signs and symptoms of aneurysm vary with its position, size, and rate of enlargement. Aneurysms of the descending and abdominal aorta are relatively rare compared with those that involve the ascending aorta and the arch.

Symptoms and Signs.—These are mainly due to pressure on surrounding structures, but in addition the patient may suffer from pain of an anginal type or attacks of cardiac asthma which are due to syphilitic aortitis. In general, aneurysms of the ascending aorta produce signs (localised pulsation, etc.) and few symptoms ; those of the arch produce many symptoms (from pressure on trachea, œsophagus, and recurrent laryngeal nerve) and few signs at first ; and those of the descending aorta may remain latent till they produce severe pain or pulmonary complications.

Aneurysm of the Ascending Aorta.—When an aneurysm occurs close above the valves there is likely to be aortic regurgitation, and ultimately rupture into the pericardium may occur. If higher up it may press upon the chest wall and eventually erode the ribs. There is dullness to the right of the sternum in the second and third interspaces, and often as the aneurysm becomes larger there may be bulging in this region with a tumour showing expansile pulsation. A systolic murmur is often heard over the aneurysm. Pain is sometimes severe.

Aneurysm of the Arch.—When the arch of the aorta is involved, symptoms and physical signs are as a rule numerous and due to pressure on surrounding structures. They may be classified as follows :—

1. *Pressure on the Trachea and Lungs.*—The aneurysm may become adherent to the trachea and produce a partial constriction. In such cases the well-known sign termed " tracheal tug " can be elicited. The patient is examined with the head thrown well back, and the observer's fingers are pressed firmly upon the cricoid cartilage ; the cricoid will be felt to be drawn

downwards with each heart beat. Pressure on a main bronchus may lead to collapse, infection, or abscess of the lung. Sometimes rupture into the lung or pleura leads to sudden death, which may be preceded by the coughing up of blood-stained sputum.

2. *Pressure on Veins.*—Compression of the superior vena cava occasionally produces congestion of the face and head, and sometimes of the arms, or collateral circulation through the mammary and epigastric veins. These phenomena are, however, much more common with mediastinal tumours than with aneurysms.

3. *Pressure on Nerves.*—The left recurrent laryngeal nerve is often involved, and this results in laryngeal irritation or paralysis of the left vocal cord. A harsh brassy cough is produced by irritation, while a hoarse voice indicates paralysis. Sometimes this may be the earliest detectable sign of aneurysm. Pressure on the sympathetic at the root of the neck may lead to inequality of the pupils and of the palpebral fissures.

4. *Inequality of the Radial Pulses.*—If an aneurysm involves the origin of the innominate artery or of the left subclavian, the mouth of the vessel may be partially obstructed ; hence the radial pulses are unequal in volume or are not synchronous.

5. *Pressure on the Œsophagus.*—Dysphagia as a result of aneurysm is very rare, as the œsophagus is usually pushed to one side rather than compressed. Rarely rupture occurs into the œsophagus with a rapidly fatal result.

Aneurysm of the Descending Thoracic Aorta.—In these cases, which are fortunately comparatively rare, the predominant feature is pain due to erosion of the spine, with irritation of nerve roots. The bodies of the vertebræ are often eroded, but the more resilient intervertebral discs remain unabsorbed. The pain is extremely severe and persistent, and is felt around the chest and upper abdomen in the course of the affected nerves. Physical signs are often indefinite, but rarely a pulsating swelling may be felt over the back, or a localised systolic murmur heard ; compression of the lung or a bronchus may give typical signs.

Aneurysm of the Abdominal Aorta.—The commonest site is immediately below the diaphragm, but the condition is far less frequent than is aneurysm of the thoracic aorta. An aneurysm high up may produce no palpable tumour, and the diagnosis is very difficult or impossible. There is severe and persistent epigastric pain, which is unaffected by diet, and can only be relieved by large doses of morphia. Most abdominal aneurysms are due to arteriosclerosis rather than syphilis.

Diagnosis.—In many cases of aneurysm the diagnosis is obvious from the presence of a pulsating tumour. When in doubt, X-ray examination should usually decide the question. The patient is best examined erect in the left lateral position. If an aneurysm is present, a shadow will be seen encroaching on the posterior mediastinum. On examination with the fluorescent screen, pulsation can be detected.

Prognosis.—About half the cases of thoracic aneurysm terminate by rupture into the lungs, pleural cavity, pericardium, or œsophagus. Death may also occur from cardiac failure or respiratory complications. If untreated, life is rarely prolonged more than a few years, but with anti-syphilitic treatment given early the outlook is considerably improved.

Treatment of Syphilitic Aortitis and Aortic Aneurysm.—Pathological changes in the aorta begin during the secondary stage of syphilis, and thorough

treatment during the primary and secondary stages of the disease are probably effective in diminishing the likelihood of the development of aortitis in later life. However, even when manifest changes have occurred in the aorta, provided the heart is not failing, the progress of the disease may be arrested by treatment with potassium iodide, bismuth, and neoarsphenamine. The patient should be kept at rest in bed and take potassium iodide in increasing doses up to 90 gr. daily, with intramuscular bismuth (0·1 gm. increasing to 0·2 gm.) at weekly intervals ; after four to six weeks of treatment intravenous injection of neoarsphenamine may be started; the first dose should be extremely small (0·1 gm.), and the dosage must be increased very gradually until doses of 0·4 gm. are being given. If this precaution is adopted there is little risk of severe reactions.

If penicillin is given the initial doses should be very small, such as 10,000 units on alternate days, owing to the risk of a Herxheimer reaction. Further increases should be made with caution.

Elderly and debilitated patients, especially if suffering from heart failure, are very unlikely to benefit from treatment either with arsenic or penicillin. If pain is severe morphia may be necessary.

For the relief of the paroxysmal attacks of dyspnœa which occur in syphilitic aortitis, amyl nitrite may be tried, but morphia and atropine are often required.

Aneurysms of Peripheral Vessels

These may be classified under the following headings :—

1. **Traumatic.**—These are of considerable importance in war wounds and stab wounds with a sharp knife. Under favourable conditions they can be treated surgically provided the anastomotic circulation is satisfactory. Proximal and distal ligature of the artery and veins is probably better than the classical proximal ligature of the artery alone.

2. **Mycotic.**—In bacterial endocarditis and pyæmic conditions, implantation of micro-organisms in the arterial wall may lead to a local erosion and weakening of the artery, which is known as a mycotic aneurysm. These are frequently multiple.

3. **Atherosclerotic.**—Peripheral aneurysms especially of the popliteal used to be very common and are still seen in elderly subjects. They are often multiple.

4. **Syphilitic.**—Such aneurysms may be found in the innominate and carotid arteries, alone or associated with the more common aortic aneurysm.

5. **Intracranial.**—These are described elsewhere (*vide* p. 594).

6. **Arterio-venous.**—This term is applied to aneurysms in which there is communication between an artery and a vein. The majority are due to gunshot wounds. The communication is sometimes large enough to produce a water-hammer type of pulse and enlargement of the heart. The high venous pressure resulting from the communication may result in greatly distended veins and much swelling of the limb, but it is surprising that this does not always occur. The treatment is the same as for other traumatic aneurysms.

THROMBO-ANGIITIS OBLITERANS

Thrombo-angiitis obliterans is an inflammatory condition that affects the arteries and veins of the limbs, and results in their occlusion by the

formation of a thrombus, which eventually undergoes organisation. The disease is practically confined to the male sex. Originally described by Buerger as occurring almost entirely among Jews, in England there is no special racial incidence. The great majority of the patients are between thirty and forty-five years of age. Occasionally it appears to have a familial incidence.

Little is known of the ætiology of the condition. Syphilis is certainly not a factor, but there is often a history of excessive smoking. From a pathological point of view, the primary change is an acute inflammatory condition of all the coats of the vessel wall. As a result thrombosis occurs ; later the clot becomes organised and the affected vessel forms a fibrous cord. Frequently areas of thrombosis may be seen in the superficial veins of affected limbs. These form localised red areas, which are tender on palpation.

The symptoms of thrombo-angiitis obliterans are due to interference with the blood supply of the affected limbs. The onset is usually insidious, and the patient's first complaint is of pain in the calves, which is induced by exercise and relieved by rest. Usually one leg is first affected, but in the course of time both become involved. In later stages there may be severe pain, burning in character, in the feet and legs, quite apart from exercise. Localised areas of thrombo-phlebitis may also occur. Less commonly, the disease may involve the arms. The patient is able to walk a certain distance, often not more than a hundred yards, without discomfort, and is then compelled to stop by the onset of pain in the calves ; after a few minutes' rest the symptoms disappear, and he is able to walk a little farther, until the pain returns. This group of symptoms is known as *intermittent claudication*, but in itself it is not characteristic of thrombo-angiitis obliterans, in fact, much the most common cause of intermittent claudication is arteriosclerosis. As the disease progresses the distance which the patient can walk before the onset of pain gradually decreases.

On examination of the affected leg the pulses in the posterior tibial and dorsalis pedis arteries cannot be felt, and the foot is livid while in the dependent position. By elevating the limb towards the perpendicular when the patient is lying down, ischæmia of the extremity is produced, and the skin becomes blanched. After some years trophic changes occur in the skin, and ultimately dry gangrene may result.

Occasionally thrombo-angiitis obliterans is associated with *erythromelalgia*, a rare condition in which there is pain, redness, and swelling in the feet or hands, particularly when the limb is in a dependent position.

Treatment and Prognosis.—In few diseases have so many different treatments, both medical and surgical, been advocated. Unfortunately there is little evidence that genuine or permanent improvement results from any one of them. Undoubtedly rest in bed is beneficial, but relapse usually occurs when the patient tries to resume a normal life. Often radiant heat or diathermy relieves the pain. The following methods of treatment have been advised :—

1. *Buerger's Passive Exercises.*—The affected limb is elevated to about 60 degrees above the horizontal and is allowed to rest in this position for the minimum time necessary to produce blanching (usually a half to three minutes). The foot is then allowed to hang down until reactionary hyperæmia or rubor sets in (usually two to five minutes). The limb is then allowed to rest in a horizontal position for about five minutes and the cycle is then repeated. The exercises are carried out for one hour at a time and should be repeated several times daily. The object is to promote collateral circulation.

2. *Alternate Suction and Pressure.*—The limb is enclosed in an airtight chamber and subjected to alternate negative and positive pressures. The apparatus required is elaborate, but favourable results are claimed after prolonged treatment.

3. *Surgical Treatment.*—Periarterial sympathectomy and ligation of the femoral vein have both proved useless, but sometimes favourable results have followed lumbar ganglionectomy, especially when vasospasm is present apart from organic obliteration of the vessels.

When pain in the foot is severe, a peripheral nerve block with alcohol or section of the sensory nerve produces anæsthesia for about six months and often gives great relief.

When gangrene occurs, especially if it is complicated by infection, amputation high up may be required.

No drugs have any specific action, but beneficial results have been claimed for alcohol, injection of tissue extracts, thyroid, acetylcholine and other substances. It is most important to avoid trauma to the feet and particularly burns by hot-water bottles. The patient may live for many years and occasionally spontaneous cure may occur, but in the majority of cases in spite of all forms of treatment the condition gradually deteriorates. Death may occur from intercurrent illnesses or toxic absorption from gangrene.

Polyarteritis (Periarteritis) Nodosa

This is a relatively rare disease affecting mainly young adult males. Little definite is known of its ætiology, but it is probable that it represents non-specific manifestations of anaphylactic hypersensitivity to a variety of antigens. Pathologically there is necrosis affecting all the coats of the artery, and vessels in all parts of the body may be involved, but particularly those of the kidneys, heart, intestines, and skin. The symptoms and signs will depend mainly on the extent and localisation of the pathological process. Thrombi may form in the lumen of the affected arteries or aneurysms may develop.

As might be expected the symptoms and signs are most protean. The most frequently encountered features are fever, often prolonged, a polymorphonuclear leucocytosis sometimes with an eosinophilia, a high blood sedimentation rate, albuminuria often with hypertension, abdominal pain, peripheral neuritis, fits, and attacks of breathlessness resembling asthma. Crops of painful subcutaneous nodules may appear which occasionally ulcerate.

Polyarteritis nodosa should always be borne in mind in cases with prolonged pyrexia and multiple symptoms of obscure origin. The diagnosis can be made by biopsy of a nodule or of muscle. In the past the diagnosis was rarely made except at autopsy, but as the disease has become more widely recognised it has been shown that at any rate a proportion recover. No specific treatment is known.

VASOMOTOR DISORDERS

Raynaud's Disease

This term is applied to a condition in which the fingers and toes are affected by an intermittent spasm of the arteries, which may ultimately reduce the blood supply to such an extent that gangrene results.

Ætiology.—Nothing definite is known of the factors that produce Raynaud's disease. It is relatively rare in males, and the onset of symptoms is usually before middle age. No constant pathological changes are found either in the central nervous system or in the vessels of the affected areas, and it is assumed that the manifestations of the disease are due to vascular spasm.

Symptoms.—The changes seen in Raynaud's disease are always symmetrical, usually affect both hands and feet, and are always worst in cold weather. Two stages are described :—

1. *Local Asphyxia.*—This most commonly affects the fingers and toes, which become cold and numb, and closely resemble the condition which may be brought about by severe cold. The vasoconstriction which produces such symptoms may last from a few minutes to several hours. The fingers, toes, and sometimes the ears and nose become intensely livid and congested ; pain is often severe, and the affected parts may become insensitive to touch. When massaged in an attempt to restore circulation they become dead-white, thus in the case of the fingers giving rise to the term " dead fingers."

2. *Local Gangrene.*—The cold asphyxiated parts become anæsthetic and black in colour as gangrene sets in. Usually gangrene is limited to the tips of the fingers and toes.

Diagnosis.—Vasomotor phenomena in the fingers when exposed to cold often result in a condition of pallor and numbness, which resembles the stage of local syncope in Raynaud's disease. Whether this condition, which is often familial, should really be classed as mild Raynaud's disease is doubtful. In many cases the tendency to " dead fingers " persists through life, and no other symptoms of the disease develop.

There is little risk of confusion between Raynaud's disease and the gangrene due either to arteriosclerosis or to thrombo-angiitis obliterans. Raynaud's disease is invariably symmetrical and affects chiefly females, while gangrene due to either arteriosclerosis or thrombo-angiitis is most often met with in males and is primarily unilateral. Intermittent claudication does not occur in Raynaud's disease.

Treatment.—No specific treatment is available, but sometimes calcium lactate in 15-gr. doses thrice daily appears to be helpful. Affected limbs should be kept at rest warmly wrapped in cotton-wool. Permanent residence in a warm climate is often beneficial. Cervical ganglionectomy may result in conspicuous improvement.

Angio-neurotic Œdema

In this remarkable but not very uncommon condition, circumscribed areas of œdema occur upon the skin and mucous membranes. Any part of the body may be affected, but most commonly the face. The swellings appear spontaneously and are sometimes preceded by itching or burning sensations ; their duration varies from a few hours to several days, but both the onset and disappearance of the œdema are remarkably rapid. Usually there are no symptoms beyond local discomfort, due to the swelling of the skin, but sometimes the attacks are complicated by severe abdominal pain and vomiting, which may simulate an acute abdominal condition. The abdominal symptoms are probably due to circumscribed œdema of the mucous membrane in the alimentary tract. If the glottis is affected there is a risk of death from suffocation.

The origin of the disease is unknown, but it is usually regarded as allergic

or as a vasomotor neurosis. In many instances it is certainly hereditary or familial, and Osler records one family in which five generations were affected.

The treatment of angio-neurotic œdema is unsatisfactory, particularly in patients with a family history of the disease. When the glottis is affected, immediate tracheotomy may be needed. Adrenaline usually gives rapid but only temporary relief. Benadryl is often effective given by mouth in repeated doses of 50 mg., as is also ephedrine. Attacks tend to be more frequent as a result of overwork and anxiety. A period of rest in bed or a holiday is often most beneficial.

Milroy's Disease

This disease is also known as Hereditary Œdema, and is nearly always hereditary or familial in origin. The swelling is confined to the legs, which may be enlarged up to the thighs ; the feet are rarely involved. It is sometimes unilateral. The œdema does not pit markedly on pressure, and there is no evidence of venous or lymphatic obstruction. The condition is painless and the general health remains unaffected, though the great weight of the limbs interferes with normal activity. A similar non-familial condition may be seen generally affecting one limb only. The firm application of crepe bandages diminishes the swelling and gives much relief. Treatment, both medical and surgical, is ineffective.

Acroparæsthesia

In this condition numbness, tingling, or " pins and needles " occur in the finger-tips without physical signs suggesting organic nervous disease. It occurs most frequently at the menopause in emotionally unstable women. Treatment is usually of little avail, but radiant heat and massage may be tried. Thyroid often proves of considerable value. The possibility of the condition being due to postural changes in the shoulder girdle must be considered.

DISEASES OF THE VEINS

Thrombosis

Inflammation or trauma of the wall of a vein leads to a local deposition of blood platelets and the formation of a clot (thrombus). Inflammation of a vein (phlebitis) may be of two kinds, plastic or suppurative, which differ widely in the symptoms produced.

Suppurative Phlebitis.—This condition is always most serious. The wall of the vein is infected from some adjoining focus of suppuration, and the thrombus which forms rapidly breaks down, and its infected fragments are discharged into the general venous circulation. This results in pyæmia and secondary abscesses, most often in the lungs.

Sinus Thrombosis is described elsewhere (*vide* p. 610).

Suppuration in the abdomen, particularly around the appendix, may lead to a suppurative pylephlebitis and multiple abscesses in the liver (*vide* p. 344).

Plastic Phlebitis.—In this condition a thrombus forms, which may ultimately undergo organisation, and the vein becomes a fibrous cord, or canalisation of the clot may open new channels for the flow of blood.

Ætiology.—Phlebitis or thrombo-phlebitis, as it is often termed, occurs not infrequently without any obvious cause, and is more common in the veins

of the legs than elsewhere. Possibly its onset is often due to focal infection, which may be quite unsuspected. Thrombosis of the femoral vein is a relatively frequent complication of typhoid fever or, indeed, of any severe general infection such as pneumonia: in such cases the left femoral vein is almost always the one which becomes thrombosed. Following parturition a similar condition may occur—phlegmasia alba dolens or "white leg." In addition to the above, thrombo-phlebitis has been attributed to many other diseases, particularly gout. Thrombosis of veins also occurs after operations, particularly pelvic operations. Thrombo-phlebitis is not uncommon in varicose veins.

Symptoms.—These will naturally vary with the site of the thrombosis. Local pain and tenderness are the earliest and most prominent features. When the affected vein is superficial there is obvious redness and œdema, but on no account should any attempt be made to palpate the vein. Thrombosis of a large vein, such as the femoral, produces marked swelling and œdema of the limb, which lasts from several weeks to many months or even years.

Some degree of pyrexia is common, but the general symptoms are slight, in contrast to suppurative phlebitis. The local pain persists for some days and then gradually subsides. Non-suppurative phlebitis has a good prognosis, provided a portion of clot does not become detached. Such an accident will produce a pulmonary embolism which may be fatal. Varicose veins with ulceration are a frequent sequel to thrombosis of deep veins in the leg.

Treatment.—Complete rest and immobilisation of the thrombosed area are essential. For the pain, sedatives such as aspirin, bromides, chloral, or even morphia may be required. Immobilisation of the affected part must be insisted on for at least four weeks, and massage or palpation must be forbidden during the same period owing to the danger of detaching a clot into the circulation. When there is no obvious cause for the phlebitis, and particularly if thromboses have been multiple, any possible source of sepsis should be eradicated.

Anti-coagulants, such as heparin and dicoumarol, have been given with a view to preventing further spread of thrombosis and decreasing risks of embolism. These drugs, however, are not without danger and should never be given unless the patient is under close observation with full laboratory facilities.

Thrombo-phlebitis Migrans.—In this condition multiple thromboses occur, usually successively, in different parts of the body. In addition to the systemic veins, those in the lungs may be affected and produce pleurisy and pleural effusion. Pyrexia of moderate degree may last for many months. Often this syndrome occurs as a secondary manifestation in carcinoma, particularly in carcinoma of the lung. Multiple venous thromboses also occur in thrombo-angiitis obliterans.

Pulmonary Embolism.—Whenever thrombosis occurs in a vein there is a risk of a portion of clot becoming detached. Should this occur, the thrombus passes through the right side of the heart and is eventually arrested at some point in the pulmonary artery or its branches. A large embolus may lodge at the bifurcation of the pulmonary artery and completely stop the circulation of blood through the lungs. Such accidents occur most often about seven to ten days after operations. The patient, who is usually convalescent, suddenly sits up in bed, becomes unconscious and convulsed, and is dead within a few minutes. There is no cyanosis, and the colour is that of a "white asphyxia."

Smaller emboli may occlude small branches of the artery and produce localised infarctions of the lung. In such an event there is sudden onset of pain in the chest, dyspnœa, and later slight hæmoptysis and a localised pleural rub. Sometimes a pleural effusion develops and is often blood-stained. If a patient with pulmonary embolism survives the first twelve hours, recovery is probable. Oxygen given through a mask or nasal catheter is extremely valuable, and morphia may be required to allay pain and restlessness. Very rarely pulmonary embolectomy has been successful.

Pulmonary emboli, which produce localised areas of pleurisy, may result from thrombosis in varicose veins. A large pulmonary infarct may produce peripheral circulatory failure, which may prove fatal (*vide* p. 419).

Arterial Embolism.—Emboli in the systemic arteries are derived from three main sources: (i) portions of thrombus from the left auricle; (ii) mural thrombi in the left ventricle after coronary thrombosis; and (iii) detached vegetations from the mitral and aortic valves. The latter accident is unusual except in bacterial endocarditis, but arterial embolism from clot formed in the left auricle is relatively common in association with mitral stenosis, especially when there is also auricular fibrillation. Emboli are especially common in the cerebrum, in the spleen, and in the kidneys, but may also occur in the mesenteric vessels, where the picture may simulate an acute abdomen, or in the arteries of the leg (less commonly the arm), or even at the bifurcation of the aorta.

The occurrence of hemiplegia after cerebral embolism is well recognised, but the occurrence of monoplegias of short duration and of other cerebral disturbances is often overlooked. With splenic infarcts, sharp pain may be the main symptom and the spleen may be palpable and tender. In the kidney, arterial embolism produces hæmaturia, naked eye or microscopic.

In the larger vessels an embolism may disintegrate after a short time, leading to relief or diminution of symptoms. The recovery may be surprisingly complete, and arterial embolectomy, even when possible, should not be undertaken lightly.

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DISEASES OF THE RESPIRATORY SYSTEM

Physical Signs

SKILL in the detection and interpretation of physical signs in the chest can be obtained only by practical instruction and experience. Accordingly it is not proposed to describe individual physical signs. Those, however, which are likely to be encountered in cases of the more important respiratory disorders will be enumerated, and where necessary their significance will be discussed under the various appropriate headings.

DISEASES OF THE NOSE

The Common Cold.—This usually originates in the nasopharynx one to five days after exposure to infection, and may spread to accessory sinuses, Eustachian tubes and middle ear, the larynx, and occasionally the trachea, bronchi, and lungs. The onset is often indicated by a sensation of chilliness which is followed by malaise, listlessness, and naso-pharyngeal catarrh. Headache is common and the digestion may be disturbed. The course varies with the severity of infection and the resistance of the individual, and the duration varies from a few days to some weeks.

Ætiology.—The liability to infectious catarrh of the upper air passages is common to all ages and races, but is relatively rare in infants and the aged. Exposure to infection is the essential factor, as shown by the freedom from colds in members of Arctic and Antarctic expeditions while out of touch with other communities. Undue exposure to cold and wet weather may often, however, be a precipitating factor.

Bacteriology.—It seems probable that a filterable virus, as yet unidentified, is the primary cause of the common cold. Secondary infection with bacteria quickly follows. Thus on culture from a nasopharyngeal swab many different organisms may be found and these may be responsible later for various complications.

Pathology.—Catarrh is the manifestation of inflammatory reaction on a mucous membrane. There occurs hyperæmia and a local invasion by leucocytes. The latter exude from the surface together with mucous cells and large quantities of mucin.

Prevention.—Some individuals are much more frequently attacked than others. In many cases this is due to local defects in the nose or throat; mouth breathers are notoriously unresistant. Other predisposing causes are unventilated rooms and excessive clothing. Above all, close contact with a sufferer in the active stage of the disease is to be avoided. It is the manifest duty of the latter to isolate himself during the first three days of the disease, and to avoid close contact and kissing until the catarrh has cleared up completely. Of prophylactic value are general ultra-violet light baths given throughout the winter. Increasing exposures up to twenty minutes for each

bath may be taken twice weekly. Inoculations of anti-catarrhal vaccine if given over a period in the autumn and winter may also be of assistance and diminish the risk of complications.

Treatment.—A hot bath, hot drinks, and rest in bed for twenty-four hours is suitable for most cases. On the first night sweating should be promoted by sleeping wrapped in a blanket and surrounded by several hot-water bottles. Opium in the form of Dover's powder (5 to 10 gr.) is a favourite remedy, as is 10 gr. of aspirin.

Swelling of the mucosa may be controlled by allowing a $\frac{1}{2}$-gr. tablet of ephedrine hydrochloride to dissolve in the mouth every three or four hours. The discomfort of nasal obstruction may be further relieved by inhalations of benzedrine. Secondary infections may be prevented or aborted by penicillin tablets (1,000 units), six to twelve of which may be dissolved slowly in the mouth singly at hourly intervals in the later stages of the illness.

Chronic Catarrhal Rhinitis.—*Ætiology.*—In patients with a low resistance, chronic rhinitis may follow a series of colds. More frequently the underlying cause is nasal obstruction, the presence of adenoids or chronic infection of an accessory nasal sinus.

Symptoms.—The symptoms are discharge of watery or mucoid secretion from the nostrils and nasal obstruction. Secondary effects may be pharyngitis, laryngitis, and middle ear disease. The mucous membrane of the nose is swollen, especially on the turbinates. At first it is red and soft; later it may become pale and tough.

Treatment.—Local causes, such as adenoids, polypi, or gross deviation of the septum, may need operative interference. In the absence of these, treatment aims at raising the patient's resistance. Most beneficial, especially for town-dwellers, is a change of climate. An autogenous vaccine prepared from organisms found on a post-nasal swab is effective in some cases.

Allergic Rhinitis.—A condition clinically similar to hay fever (*vide* p. 478), is to be found in those who are sensitive to foreign proteins. The nasal mucous membrane is swollen, pale, and hypertrophic. Nasal polypi frequently develop, and chronic secondary infection is common. The best treatment is a combination of desensitisation and surgery.

Epistaxis.—Epistaxis, or bleeding from the nose, is common in young children and in the elderly. In the former, it is usually due to some local cause such as acute rhinitis or trauma, while in old age it is more often due to remote causes such as benign hypertension, chronic nephritis, and hepatic cirrhosis. It occurs also in association with valvular disease of the heart, and various forms of anæmia, uræmia, purpura, and scurvy. It is a common symptom in the early stage of enteric fever.

The bleeding arises as a rule from vessels on the anterior part of the nasal septum. In patients suffering from hyperpiesis, heart disease, or uræmia it may be beneficial; in others the loss of blood may do serious harm. Epistaxis is common in hereditary telangiectasia (*vide* p. 278).

In order to stop the bleeding the patient should be kept still with the head raised. An ice-bag is applied to the back of the neck, and the nostril plugged with cotton-wool soaked in solution of adrenaline 1 in 2,000.

Intractable epistaxis is best controlled by a pneumatic plug. This consists of an india-rubber finger-stall, inside which is sealed the end of a soft catheter. The finger-stall is inserted into the nose, and inflated through the catheter, which is then clamped. If bleeding continue from a localised area,

cauterisation with an electric cautery or a stick of silver nitrate should be tried. Blood transfusion may occasionally be required.

DISEASES OF THE TONSILS

Acute Tonsillitis.—*Ætiology.*—This may occur sporadically or in epidemics; the sporadic variety is seen chiefly in persons with chronic enlargement of the lymphoid tissue of the throat. Epidemics are common in institutions, especially hospitals. The causative organism varies but is often a hæmolytic streptococcus which is directly communicated from case to case. The disease, though common in children and young adults, is rarely seen in infants or the aged.

Morbid Appearance.—The tonsils become red and swollen, the crypts fill with exudate and debris which project from the orifices as pale cheesy masses. The exudate from several crypts may coalesce to form a yellowish-grey patch. The surrounding pharynx is more or less inflamed.

Symptoms.—There is a sudden onset with chill, aching pain in the back, and headache. The temperature may rise to 104° on the first day. The face is pale, breath offensive, tongue heavily coated. The cervical lymph glands may become tender and enlarged. The urine is concentrated and sometimes contains a trace of albumin. The throat feels sore and there is pain on swallowing.

As a rule, the temperature falls after three or four days and health is quickly restored. Serious complications, such as septicæmia, acute otitis media, acute nephritis, acute rheumatism and rheumatic carditis may occur, especially in children. Less serious complications are a diffuse erythema simulating scarlet fever, fibrositis, and erythema nodosum.

Diagnosis.—The most certain method of distinguishing tonsillitis from diphtheria is by bacteriological examination which will establish the causal organism, and which should, whenever possible, be a routine investigation for these cases. However, in diphtheria a firm ashy-grey membrane forms, more commonly on one than on both tonsils, soon extends to the faucial pillars and uvula, and is fairly sharply limited in extent, whereas the exudate of follicular tonsillitis is loose and yellow, involves both tonsils diffusely, and rarely extends beyond them. When diphtheria is suspected, treatment must not be delayed pending the report on a swab. Cervical adenitis is more and fever less striking in diphtheria than in tonsillitis.

Treatment.—The patient should be kept in bed and the diet limited to liquids and jellies. Free action of the bowels should be obtained by means of calomel and salines. Warm applications externally to the throat give relief, and powdered aspirin may be insufflated to relieve pain. If sleep is disturbed, Dover's powder, 5 to 10 gr., may be given at night. Chemotherapy should not be employed in a haphazard fashion. If the infecting organism is shown to be susceptible it is desirable to give the appropriate sulphonamide drug in full doses (*vide* p. 7). In the presence of severe infection, or where the organism proves sulphonamide-resistant, penicillin should be used ; 1,000-unit lozenges dissolved slowly in the mouth every hour, and in addition 50,000 units intramuscularly every three hours of the daytime may be used and continued for two days after the fever has abated.

Vincent's Angina.—*Ætiology.*—This is an ulcero-membranous affection of the throat and mouth, due to combined infection with the fusiform bacillus and spirillum of Vincent. Infection can be transmitted by drinking utensils.

Symptoms.—The lesions may be multiple, resembling follicular tonsillitis, or a single " wash-leather patch " may form on one tonsil. The patch is raised and irregular, and bleeding occurs when the slough is detached. The membrane may spread to the fauces or along the gums. The cervical glands enlarge on the side affected. The breath is offensive, dysphagia is common, but pyrexia and constitutional disturbance are very variable. In some cases the slough separates after a few days, and the ulcer quickly heals. In others the lesion persists for many weeks.

Diagnosis.—The spirillum, together with the fusiform bacillus, may be identified by microscopical examination of a smear, although it does not grow on ordinary culture media. The lesion may simulate diphtheria, but there is not the same constitutional disturbance. A similar appearance is sometimes seen in agranulocytosis, glandular fever, and in the pharyngeal necrosis associated with the leukæmias. The chronic form may resemble the mucous patch or tertiary ulcer of syphilis. In cases of difficulty the Wassermann reaction should be done.

Prognosis.—There is no danger except when Vincent's angina supervenes on scarlet fever, diphtheria, or some other acute fever.

Treatment.—An abundant varied diet is desirable. Extra vitamin B_2 (nicotinic acid, 250 mg. daily) and vitamin C may be of help. Penicillin is specific, and is best given locally in 1,000-unit lozenges dissolved slowly in the mouth every hour. The disease is commonly cured in two days, though systemic penicillin may be needed in a few cases. In chronic cases, diseased teeth should be extracted.

Peri-tonsillitis or Quinsy.—*Ætiology.*—A quinsy is generally preceded by acute tonsillitis, and results from the inflammation spreading to the tissues outside the capsule of the tonsil.

Symptoms.—The condition is generally unilateral, and the swelling pushes the tonsil and soft palate downwards. An abscess forms, and if not incised may burst in four to six days. At first the patient complains of sore throat and great pain on swallowing. Later the cervical glands enlarge and the jaw becomes fixed. Cases have ended fatally from œdema of the larynx, from suffocation brought about by bursting of the abscess during sleep, or from hæmorrhage.

Treatment.—In the early stages this is the same as that for acute tonsillitis. A quinsy will usually be aborted by sulphanilamide or penicillin therapy if these are applied early. If pus has formed, it should be evacuated. The soft palate is painted with cocaine, and a guarded bistoury is thrust into it at the point of maximum swelling above the tonsil. Local and intramuscular penicillin, as in acute tonsillitis, should be employed concurrently. A hot compress to the neck affords some relief.

Chronic Tonsillitis.—In many children the tonsils enlarge during the period of decay of the milk teeth. This enlargement may persist as a simple hypertrophy in conjunction with adenoid overgrowth, and accentuate the obstruction due to the latter. Removal of the adenoids and establishment of nose breathing will often bring about subsidence of the hypertrophy.

Chronic Septic Tonsillitis is to be distinguished from the above. In this variety the tonsils are not necessarily larger than normal, and in some

instances they are contracted and fibrous. The crypts are filled with offensive cheesy material consisting of epithelial cells, pus cells, and organisms. In some cases concretions form, known as tonsilloliths.

Symptoms.—Locally the condition gives rise to frequent " sore throats " and enlargement of cervical glands. Constitutional disturbance is shown by bouts of pyrexia, anæmia, dyspepsia, and sometimes by fibrositis or polyarthritis.

Treatment.—Carious teeth should be extracted and other septic foci about the mouth and nose must be eradicated. If the tonsils do not regain a healthy appearance, but still harbour material after the above measures have been carried out and a suitable period allowed for recovery, then the tonsils should be enucleated. The tonsils are useful organs and form part of the defence against infection ; they should be sacrificed, therefore, only when it becomes clear that they cannot be restored to a healthy condition.

Agranulocytic Angina.—*Vide* p. 274.

Adenoid Vegetations

Ætiology.—The condition occurs in children, chiefly between the ages of three and six years, but is met with occasionally in young infants. It is especially common in England, perhaps owing to the cold damp climate.

Morbid Appearance.—The vegetations form a foliated mass on the roof of the nasopharynx. They may extend down the lateral walls, cover the openings of the Eustachian tubes, and partially occlude the posterior choanæ. The lymphoid masses are covered by squamous or columnar epithelium, and there is usually an associated hypertrophy of the tonsils and cervical adenitis.

Symptoms.—As a result of post-nasal obstruction, the child becomes a mouth breather. The " adenoid facies " is characterised by the open mouth, projecting upper lip, narrowed nostrils, and high-arched palate. Associated developmental abnormalities of the chest occur, including " pigeon " and " funnel " breast.

Other symptoms of adenoids are backward mentality and inability to concentrate, impairment of hearing, headache, night terrors, and enuresis. Children having this complaint are especially liable to recurrent colds, chronic tonsillitis, otitis media, and chronic bronchitis.

Treatment.—This is surgical, the adenoids being removed by means of a curette. After operation, breathing exercises should be practised in order to teach the child to breathe through the nose. Cod-liver oil should be taken together with a good mixed diet, and exercise in the open air encouraged.

DISEASES OF THE LARYNX

Acute Catarrhal Laryngitis.—*Ætiology.*—This condition may be due to the same causes as acute rhinitis ; it also follows inhalation of hot or irritating vapours. An attack may be provoked by over-use of the voice as in shouting. It is a common symptom in measles and influenza, and may occur in patients with pulmonary tuberculosis quite apart from tuberculous ulceration of the larynx.

Morbid Appearance.—The mucous lining of the larynx is swollen and hyperæmic ; the cords are pink or red, and there is usually infiltration of the

submucosa and muscles resulting in lack of tension of the cords in phonation. The sputum is viscid and may be streaked with blood.

Symptoms.—In an adult the chief complaints are of partial or complete loss of voice, an irritating cough, and a feeling of soreness in the larynx. There may be slight pyrexia and malaise. In the majority of cases the symptoms pass off in the course of one or two weeks.

In the child there are dangers due to the comparative narrowness of the glottis and the tendency to reflex spasm. During the day the symptoms are seldom alarming, but at night the child may wake in a terror with loud crowing inspiration (laryngitis stridulosa), urgent dyspnœa, and cyanosis.

Treatment.—The patient should remain in bed, be forbidden to speak, guarded from draughts, and the atmosphere of the room should be kept moist by means of a steam-kettle. In a majority of cases the organism concerned is sensitive to penicillin, which may best be given by inhalation from a Collinson or Deedon inhaler in doses of 100,000 units thrice daily for three or four days. The cough should be checked by a sedative linctus or lozenge. In children, relief may be obtained from hot compresses to the front of the neck, and by a mixture containing 1 gr. of potassium antimony tartrate, or by $\frac{1}{30}$ gr. apomorphine, injected hypodermically. The child should take small doses of chloral and potassium bromide. In extreme cases intubation or tracheotomy may be necessary.

Membranous Laryngitis.—This is almost always diphtheritic, though rarely it occurs with other acute infections. The case should be treated as one of diphtheria even in the absence of bacteriological confirmation.

Œdema of the Larynx.—*Ætiology.*—Local causes include acute and chronic infections, mechanical or chemical trauma, or spread of infection from, for example, cellulitis of the neck. General causes are nephritis, which accounts for over 10 per cent. of cases, heart failure, superior vena cava obstruction, beri-beri, and amyloid disease, iodine sensitivity, or an attack of angio-neurotic œdema in the tissues of the larynx.

Morbid Anatomy.—The œdema affects chiefly the loose submucosa of the epiglottis, the aryepiglottic folds, and the ventricular bands ; the vocal cords are little affected. In the septic cases the fluid is purulent, in the others serous.

Symptoms.—The patient complains of a feeling as though there were a foreign body in the throat. There is difficulty in swallowing, the voice becomes muffled, and at any time obstruction may ensue with inspiratory stridor. With the laryngoscope the mucous membrane looks pale and tense, the epiglottis swollen and erect, and the aryepiglottic folds form ovoid tumours. Without a laryngoscope these swellings may be detected by examination with the finger. The onset may be sudden, and fatal obstruction may occur in less than half an hour ; in other cases the condition arises gradually, but even in these there is danger of a sudden exacerbation.

Treatment.—Those measures employed for acute laryngitis are commonly advantageous. Fluids may be given by rectum. To prevent spasm, atropine and potassium bromide are given every four hours. Pilocarpine, $\frac{1}{8}$ gr. injected thrice at intervals of twenty minutes, has led to rapid relief. Benadryl (50 mg.) or antistin (100 mg.) may be used, but if dyspnœa develops tracheotomy should be employed without delay.

In cases due to angioneurotic œdema a subcutaneous injection of 7 minims of a $\frac{1}{1000}$ solution of adrenaline should be given, and a spray of 5 per cent. cocaine and $\frac{1}{2000}$ adrenaline may be used subsequently. In œdema due to

iodism, large doses of sodium bicarbonate should be given. In cases due to other causes of œdema, such as heart failure, therapy for the primary disorder will be employed, and in a proportion of these a mercurial diuretic such as mersalyl will be most effective.

Chronic Laryngitis.—*Ætiology.*—This may supervene on acute catarrhal laryngitis, or it may be caused by chronic sepsis in the nose, adenoids, the tonsils, or mouth. Other factors are over-indulgence in alcohol or tobacco. It is also caused by faulty voice production in those who speak in public, *e.g.*, "clergyman's throat," and is common in costermongers, actors, and singers.

Symptoms.—A frequent irritable cough and scanty viscid sputum are present; the voice is husky or there may be aphonia. The loss of voice is usually most complete in the mornings, and phonation becomes easier when the patient has used the voice for a time, neither of which features occur in hysterical aphonia.

With the laryngoscope, in the slighter cases, the cords are seen to have lost their clear white definition, and to be slightly swollen. In more advanced cases the mucous membrane of the larynx may show local or general thickening, or the cords themselves may be thick and irregular, as described by Virchow under the name pachydermia laryngis.

Diagnosis.—In every case the possibility of tuberculous laryngitis (*vide* p. 102) must be borne in mind, and careful examination of the lungs and sputum should be made. In patients above the age of forty the condition may be due to carcinoma. In this case the thickening and impaired mobility will be for the most part unilateral.

Treatment.—The voice must be rested, and sepsis in the nose, throat, and mouth eradicated. Alcohol and tobacco are forbidden. A change of climate is often of great value. Cough is subdued by administration of codeine, taken in $\frac{1}{2}$-gr. tablets. In severe cases it may be necessary to spray the cords with 25 per cent. argyrol.

Syphilis of the Larynx.—Syphilitic changes in the larynx are by no means rare. Secondary syphilis may give rise to a mild catarrhal condition, but tertiary lesions are much more serious. They usually take the form of gummata in the submucous tissue at the base of the epiglottis, and may break down, leaving deep ulcers, or in their healing give rise to fibrous cicatrices which bind down the epiglottis and lead to such stenosis that tracheotomy becomes necessary. Congenital syphilis gives rise to similar damage. Neither cough nor pain are commonly present.

Treatment is the same as that of syphilis in its other manifestations, except that potassium iodide should not be given early. Mercury alone suffices to clear up the swelling.

New Growths of the Larynx.—*Innocent tumours* of the larynx may occur at any age. The commonest type is the papilloma, which appears as a warty outgrowth, often multiple, on the cords or ventricular bands. Fibromata and mucous cysts are less common. The first symptom is alteration of the voice when the cords are implicated. A large tumour will cause dyspnœa by obstructing the airway. The treatment is operative removal.

Malignant growths occur more frequently in men than women, usually after the age of forty. Persistent hoarseness in an elderly patient should suggest the presence of a carcinoma. The commonest growth is squamous-celled carcinoma, seen as a single warty tumour on one cord, the movement of

which becomes impaired. Death results from ulceration and hæmorrhage, or from septic complications such as cellulitis or broncho-pneumonia.

Treatment.—In early cases a complete excision of the larynx may preserve life for years ; in many cases great relief may result from the local application of radium.

DISEASES OF THE TRACHEA

Both acute and chronic tracheitis as a rule occur in association with similar inflammation of the bronchi. Tracheitis may also develop in cases of diphtheria, typhoid, influenza, and measles, while a particularly acute form of the disease may follow the inhalation of an irritant such as mustard gas. Acute tracheitis gives rise to a sensation of soreness behind the manubrium and sternum, and to a paroxysmal noisy raucous cough productive of traces of sputum which are not infrequently blood-stained. The clinical course, prognosis, and treatment of simple forms of tracheitis are essentially those of the corresponding bronchial infection. Tracheitis associated with specific fevers may need special appropriate therapy for which the sections concerned should be consulted.

Tuberculous tracheitis is occasionally found in association with tuberculous bronchitis, and leads to local ulceration and formation of granulation tissue. The trachea may sometimes be involved both in congenital and acquired syphilis, the typical lesion being a gummatous ulcer which may progress to stricture formation. Vigorous antisyphilitic measures are required at an early stage, though, as in the case of the larynx, iodides should be used with caution. Leprosy and scleroma may also cause stricture of the trachea.

These granulomatous lesions, rare primary, innocent, and malignant tumours, more frequently adjacent neoplasms, such as retrosternal goitre, and inhaled foreign bodies, are sometimes productive of obstruction of the lumen of the trachea.

The symptoms and signs depend upon the extent of the obstruction and upon the rapidity of its development. Thus a foreign body may cause intense distress, infection, cough, increasing dyspnœa which is predominantly inspiratory, stridor, and cyanosis, and may rapidly be fatal. On the other hand, a slowly progressive stricture gives rise to cough, slowly increasing dyspnœa, and stridor, which is at first only noticeable during sleep.

The diagnosis is confirmed by bronchoscopy, and this procedure is essential for therapy in some instances, for example, an impacted foreign body. Treatment is otherwise that of the underlying disease, and may be in part surgical.

DISEASES OF THE BRONCHI

During expiration the muscle of the bronchi normally contracts so that they shorten and become narrower, while in inspiration the musculature relaxes, permitting elongation and widening. With partial bronchial obstruction, therefore, inspiration tends to be less impaired than does expiration, and there is a tendency for the distal area of lung to become distended and ultimately emphysematous. When bronchial obstruction is complete the corresponding area of lung collapses completely as a result of absorption of air in the alveoli by the circulating blood. A further consequence of bronchial obstruction is a proportionate failure of excretion of sputum which invariably

results ultimately in infection of the bronchi, bronchioles, and lung of varying severity. The infection commonly occurs while obstruction is partial, it always follows within a few days of complete obstruction of a bronchus, and while it may remain limited to the segment of lung concerned, extension of the process is by no means uncommon.

Bronchial obstruction may be widespread, as in acute and chronic bronchitis or asthma, may involve bronchioles or terminal tubes, as in bronchiolitis and broncho-pneumonia respectively, or may be localised to a site on a main bronchus. In the last instance it may be caused by viscid sputum, blood, or an inhaled foreign body, by bronchial neoplasms, or by pressure from adjacent tumours, including aneurysm and enlarged mediastinal lymph glands. Localised stricture of a bronchus arising from trauma, kinking, or chronic inflammation have the same consequences.

Additional sequelæ of bronchial obstruction with its induced atelectasis and pulmonary infection are bronchiectasis, bronchiolectasis, various forms of pneumonia, lung abscess, and their complications. The symptoms, physical signs, radiological appearances, and other features of the disorder are listed under the headings of these various conditions with which it is associated.

BRONCHITIS

Bronchitis is the commonest disease of the respiratory tract. It may be defined as an inflammation of the lining membrane of the larger and medium-sized bronchi, and may be set up by inhalation of irritating vapours, but in the great majority of cases it is the result of infection. The air passages are provided with an elaborate defence against invasion by foreign organisms. Their lining membrane secretes mucus, which is in itself bactericidal. This mucus is continually moved upwards and ejected by the action of the ciliary processes of the bronchial mucous membrane. Removal of the secretion, together with engulfed organisms and other particles, is aided by the respiratory movements. Moreover, the epithelial lining has a free blood supply so that, at need, a plentiful supply of leucocytes will pass from the capillaries to the epithelium to aid the latter in its combat with infecting bacteria. The inspired air, before reaching the lungs, comes in contact with the mucous membrane of the nose and throat, and being deflected at the numerous folds and angles in these passages, is warmed, moistened, and cleansed of dusty particles which adhere to the moist epithelium. The ring of lymphoid tissue in the upper end of the pharynx is an important element in the defence against infection. The sensitive reflex of the glottis prevents the entry of foreign bodies from the pharynx, and the cough reflex aids in the removal of material from the larger tubes.

Bronchitis results either from a failure of the defences of the respiratory tract as a result of their being overwhelmed by a virulent infection, or by depression of the resisting power as a result of exposure to cold, or as a consequence of some defect in the anatomical structures. In some cases infection is carried to the bronchi by the blood stream.

Acute Bronchitis

Acute bronchitis, or catarrhal inflammation of the larger and medium-sized bronchi, is not often a serious disease except in infancy and old age.

Ætiology.—Acute bronchitis often follows from "catching cold." The inflammatory process extends from the nasal fossæ down the pharynx and trachea to the bronchial mucous membrane. It is also a prominent feature in many influenzal epidemics, it follows the inhalation of irritant vapours and organic dust, and occurs in association with other diseases, especially measles, whooping-cough, gout, and malaria.

Infecting organisms include pneumococci, streptococci, *M. catarrhalis*, and *B. influenzæ*.

Morbid Anatomy.—The mucous lining of the bronchi is congested, œdematous, and sometimes ulcerated, while on its surface there is a great excess of mucus mixed with more or less pus. Microscopically the goblet cells are seen to be distended, while the walls of the tubes are infiltrated with leucocytes.

Symptoms.—At the onset there is a feeling of oppression and languor, together often with myalgia. The temperature and respiration rate are only slightly raised. The cough is at first barking, severe, and painful, the expectoration scanty and viscid. After a day or two the sputum becomes more plentiful and purulent and the cough easier, with great relief to the patient. As a rule the symptoms subside after a week, and recovery is more or less complete at the end of a fortnight. In the case of infants and of feeble elderly subjects there is a danger of the smaller tubes becoming blocked with secretion and of broncho-pneumonia resulting.

Physical and Radiological Signs.—The tongue is usually coated and the voice husky. As regards the chest, signs are often surprisingly slight. In most cases a few high- and low-pitched rhonchi are heard accompanying inspiration, scattered over both lungs, and moist râles may be detected chiefly over the lower lobes. Radiologically active vascular congestion may be apparent.

Diagnosis.—There is little difficulty in diagnosing acute bronchitis. It may, however, be only a feature heralding the onset of some more serious disease such as typhoid, measles, whooping-cough, or broncho-pneumonia.

Treatment.—The patient should stay in bed and keep warm. A steam-kettle relieves the sensation of rawness in the chest as also do inhalations from ½ dr. ol. pinæ sibericæ in 1 pint of nearly boiling water. Dover's powder or syrup of codeine should be given at night, and during the first few days a mixture containing 3 to 5 gr. of potassium iodide or 12 minims of vinum antimoniale may be used to loosen the expectoration. An alkaline expectorant should be given as soon as the cough is productive. Penicillin, 300,000 units daily, given frequently as a fine spray from an atomiser is a most effective treatment. The same dose by three intramuscular injections is also satisfactory, or the sulphonamides may be used. In either case bacteriological confirmation is desirable, though therapy need not be delayed on this account.

In children, relief is obtained by rubbing the chest with a stimulating liniment such as camphor. If there is much secretion, and expectoration does not keep pace with it, vomiting should be induced by administration of a tablespoonful of tincture of ipecacuanha.

Bronchiolitis.—Bronchiolitis or capillary bronchitis is an acute inflammatory process involving the smallest air tubes. It is a dangerous complication of acute bronchitis not uncommon in young children; it is relatively rare in adults, but was the cause of death in many of the cases of influenza in the pandemic of 1918.

Symptoms.—As a rule the symptoms of inflammation of the larger tubes

are present for several days before the bronchioles become affected. When the smallest tubes become involved they are quickly obstructed by secretion and swelling of the walls, and a profound change comes over the clinical picture. Dyspnœa and tachycardia become marked. The face takes on a peculiar lilac-tinted lividity; the patient becomes exhausted, and mental disturbance is shown by delirium or coma. Anoxia and peripheral circulatory failure are the major causes of these symptoms.

Physical and Radiological Signs.—On examination of the chest the intercostal spaces are seen to fall in during inspiration. Areas of impaired resonance may indicate collapse of portions of the lungs. Râles are to be heard over the lungs, while widespread acute emphysema greatly reduces breath sounds. X-ray appearances are very variable; in a mild case only a few fine scattered opacities of lobular collapse will be seen, but in more serious examples of the disease the appearances more nearly resemble those of broncho-pneumonia, with multiple patchy ill-defined shadows particularly involving the bases. In addition, the increase in chest size and translucency characteristic of emphysema will be found.

Prognosis.—In acute cases the outlook is extremely grave, but recovery is not uncommon in those of a less fulminating type. Broncho-pneumonia is a common sequel, less often there occurs the development of a permanent dilatation or bronchiolectasis.

Treatment.—An abundant supply of fresh air is essential. The patient should be nursed as far as possible outdoors. Oxygen should be administered continuously by means of a tent, mask, or nasal catheters. Venesection may be beneficial; hypodermic injections of atropine are given at regular intervals in order to diminish the quantity of secretion and so relieve the obstruction in the bronchioles. Sulphonamides and penicillin have yet to be proved to be of value. Therapy is otherwise that of bronchitis.

Chronic Bronchitis

Ætiology.—Chronic bronchitis is a common affliction in those over forty, and it is occasionally encountered in the young. It occurs most frequently in cold damp climates among those who live in towns; at first they are affected only in the cold season, but as time goes on the condition lasts longer and longer into the summer until ultimately it continues all the year round. It may follow several attacks of acute bronchitis, and may be consequent on some structural defect of the lungs, such as emphysema, which diminishes their mobility, in turn producing stagnation of the bronchial secretion and infection of the bronchi themselves. A liability to chronic bronchitis is inherited, and it is a common disease among Jews.

Other conditions which favour the development of chronic bronchitis are spinal curvature, fibrosis following unresolved pneumonia, obesity, and asthma. In the absence of any of the above, search should be made for some focus of infection from which organisms may be entering the respiratory passages. Such foci may be present in oral sepsis, disease in the nasal fossæ or accessory sinuses.

Morbid Anatomy.—The lungs are emphysematous, the mucous lining of the bronchi may be thick and granular, but in some cases it is atrophied. Bronchiectasis may coexist.

Symptoms.—A major complaint is of shortness of breath on exertion.

This is due partly to the associated emphysema and partly to the presence of excessive secretion in the tubes. This secretion becomes churned into a foam by the air passing through the bronchi, and interferes with the entry of the inspired air into the air sacs. The capacity for work and exercise is greatly diminished by the inefficient intake of oxygen, as well as by the absorption of toxins from the infected secretions. The cough is apt to be very troublesome during the night, disturbing sleep. The lack of sleep together with dyspnœa and toxæmia sometimes leads to emaciation. The sputum consists chiefly of translucent gelatinous mucus, which in town dwellers is stippled with black carbon particles. During exacerbations of the disease, admixture of pus renders the sputum yellow or green, and streaks of blood may appear as a result of oozing from the congested or ulcerated mucosa.

Asthma frequently complicates the disease, and in these cases status asthmaticus is liable to develop. Sometimes the association of sclerotic changes in the pulmonary arteries and arterioles with emphysema leads to pulmonary hypertension and later to hypertrophy and failure of the right ventricle.

Physical and Radiological Signs.—The signs are usually trivial in proportion to the symptoms. Emphysema is recognised by the changes described elsewhere (*vide* p. 458). The bronchitis reveals itself by rhonchi and moist râles heard chiefly over the lower lobes ; it may be necessary to make the patient cough and take deep breaths before these are elicited. Associated bronchial spasm gives rise to widespread musical rhonchi and prolonged expiration. In advanced stages of the condition, cyanosis is evident, especially at the ears and finger-tips, and the latter become clubbed. The radiological appearances are those of emphysema, together sometimes with vascular engorgement.

Treatment.—Sepsis in the mouth and nasopharynx must be dealt with. In many cases effective respiration and removal of bronchial secretion can be aided by breathing exercises. Expectoration should also be promoted by the occasional use of the following mixture, which should be taken with an equal quantity of hot water : sod. chlor. gr. iii, sod. bicarb. gr. v, spt. chlorof. ℥v, aq. ad ℥i. The infection may be ameliorated temporarily by inhalations of penicillin spray, 100,000 units daily, from an atomiser, for example, prior to an operation. The patient during the winter months should take the following mixture regularly : tinct. stram. ℥xv, ammon. carb. gr. iii, sod. bicarb. gr. x, pot. iod. gr. v, syrup, aurant. ℥ss, aq. ad ℥ss. Codeine may be given freely in doses of ½ to 1 gr. by mouth to reduce the cough at night. Cod-liver oil is useful in improving the general health.

By these means the inflammatory process may be reduced to a minimum, and associated bronchial spasm can be relieved by ephedrine tablets, ½ gr. two or three times daily. These patients, in general, are far healthier in a warm equable climate, and should if possible avoid the English winter. Failing this a warm, dry occupation and abstention from tobacco and alcohol are important.

Plastic Bronchitis.—This is an uncommon affection characterised by the formation of casts in the bronchial tree. The patient is troubled by an irritating cough which increases in severity for several days. At last, in a paroxysm of coughing, a white muco-purulent lump is expectorated, and this on being unrolled in water is found to contain the hollow cast of a bronchus with dichotomous branching. The cast consists of mucin ; after it has been

expectorated the symptoms cease, but often recur at intervals of months or years.

The condition is seldom serious, and no treatment is known to be curative. The cause is unknown, but similar mucinous casts are sometimes expectorated after paracentesis for pleural effusion, or occur in association with pneumonia, pulmonary tuberculosis, or mucous colitis.

BRONCHIECTASIS

The ætiology of bronchiectasis is uncertain. Dilatation of the bronchi may occur in the main trunks, in smaller branches, and the bronchioles are often involved. In extent it may be widespread throughout the lungs, or limited to a few tubes in one lobe. Most commonly the lower lobes are involved. Dilatation of the larger trunks tends to be cylindrical or fusiform, while smaller bronchi and bronchioles which have little muscle and no cartilage in their walls dilate to form saccules.

Complete bronchial obstruction gives rise to atelectasis of the lung, which in turn causes a considerable fall in the intrapleural pressure, since the volume of the contents of a semi-rigid structure has been diminished. The decrease in volume is partly made good by movement inwards of the thoracic parieties, by displacement of the mediastinum towards the atelectatic lung, by compensatory emphysema of the residual lung and by dilatation of the bronchi within the atelectatic area. Clinically, furthermore, the association of bronchiectasis with infections such as chronic nasal sinusitis, whooping-cough, the pneumonias, particularly broncho-pneumonia, lung abscess, and tuberculosis, is well recognised. Since, if bronchial obstruction persists, pyogenic infection within the atelectatic sector quickly follows, inflammatory damage to the stretched bronchial wall may occur, and may result in permanent dilatation even if the obstruction proves to be temporary and the lung re-expands.

Basal bronchiectasis occurs more commonly in the left than in the right lung. This is probably due to the anatomical relations of the left main bronchus, which render it more susceptible to occlusion by compression when, for example, tuberculous mediastinal lymphadenitis develops.

Finally, congenital cystic disease of the bronchi, which is probably less rare than has hitherto been believed, has many characteristics (*vide* p. 456) so similar to those of acquired bronchiectasis as to suggest that a developmental abnormality may play a part in the ætiology of the latter.

Morbid Anatomy.—When the affected lung is incised and the cut surface inspected, the dilated tubes are seen with their congested mucosa projecting. Microscopical examination shows chronic inflammation of the bronchial wall, while the epithelial changes are variable since replacement by granulation and fibrous tissue, metaplasia, or persistence of ciliated epithelium may be found. In the area affected the lung may be atelectatic, and often evidence of chronic pneumonia is shown together with a more or less extensive fibrosis. Emphysema in the peripheral and uninvolved areas of lung is always present.

Symptoms.—It is probable that many patients in whom bronchial dilatation is present continue without symptoms for long periods of time. Not infrequently the main symptom is recurrent, often severe, hæmoptysis. Sooner or later, infection within the dilated tubes dominates the clinical

picture, and then periodic attacks of violent cough productive of large quantities of purulent sputum result. The most severe paroxysm as a rule occurs with change in posture, for example, when the patient awakes in the morning, and such an attack often culminates in vomiting. Periods of freedom from symptoms may occur, for example, in warm weather, though these tend to decrease. Intercurrent infection, or an exacerbation of the existing infection, may easily at any time give rise to bronchitis, pneumonia, pleurisy, or empyema. With time the sputum becomes fœtid and the breath most offensive. In such cases a chronic septic pneumonia may lead to cachexia. In unilateral bronchiectasis the patient lies on the affected side, for his sleep will not be disturbed by cough as long as the secretions remain in the dilated and insensitive tubes. He may live many years. Death may result from toxæmia, broncho-pneumonia, cerebral abscess, or amyloid disease.

Physical and Radiological Signs.—If the disease is minor in degree and remote from the surface, there may be no abnormal signs, and diagnosis must be based on the symptoms. Where there are saccular dilatations near the chest wall, clear signs of cavitation with numerous rhonchi and coarse râles may be obtained. Associated atelectasis and fibrosis result in mediastinal displacement towards the affected side, impaired movement and percussion note, and a diminished air entry, which may be bronchial in type. The fingers and toes may be clubbed, and the nails cyanosed, curved, and thick. Sometimes there is hypertrophy of the phalanges, wrists, and ankles—" hypertrophic pulmonary osteo-arthropathy."

Radiologically lobar or lobular atelectasis may be shown, and not infrequently the outline of the hollow dilated bronchi may be seen. On other occasions patchy consolidation may be the only demonstrable abnormality, while often bronchiectasis is not revealed by X-ray examination unless the bronchi are outlined by radio-opaque iodised oil. The technique of bronchography can only be learnt by practical experience, and therefore no attempt is made to describe the various methods adopted. As a preliminary, however, it is essential to exclude cocaine and iodine sensitivity, and it should be remembered before attempting the procedure that a considerable proportion of the opaque oil may be retained indefinitely in the lung and thus detract from the value of subsequent X-ray examination. Bronchography is most useful if at one time the entire bronchial tree of one lung only is delineated, for in this way both lateral and postero-anterior films will be of value in localising the disease. Bronchoscopy is a most desirable investigation in many cases of bronchiectasis, for a foreign body, bronchial stricture, or neoplasm may thereby be revealed and appropriate therapy instituted.

Treatment.—Early efficient treatment of such disorders as massive collapse and broncho-pneumonia will reduce the incidence of bronchiectasis. In early cases residence in a warm dry climate, the avoidance as far as possible of intercurrent infections, therapy for coexistent disease such as nasal polypi or sinusitis, and the practice of breathing exercises are important. Once sepsis has become established, medical therapy can only be palliative, and is designed to keep the cavities as clean as possible. The secretions must be emptied out several times a day by postural drainage, the patient with basal disease lying on an inclined plane head downwards and coughing ; continuous postural drainage is greatly facilitated by the use of the Nelson tilting bed. Penicillin spray inhalations are of temporary benefit, particularly as a preoperative measure. If the severity of the symptoms justifies radical

treatment, the method of choice is excision of the affected lobe or lobes. This must only be undertaken after complete bronchography has demonstrated that the diseased bronchi are entirely or almost entirely restricted to the area to be removed at lobectomy or pneumonectomy. This form of therapy should rarely be attempted in patients over the age of forty-five, or in those in whom cardio-vascular disease or extensive emphysema coexists.

CONGENITAL CYSTIC DISEASE OF THE BRONCHI

In the last decade an increased interest in the problem and the widespread use of radiology in the investigation of diseases of the chest have made it seem likely that cystic disease of the bronchi of congenital origin exists. Isolated cases in which the disorder has occurred in the fœtus are on record, and it is thought that arrest or abnormal development of the lung buds at an early stage may account for cyst formation. Cystic dilatation of bronchi, however, can undoubtedly be acquired. Pathological examination, however, does not as yet permit a distinction between congenital and acquired cystic disease to be made.

In the existing state of our knowledge it is convenient to adopt a clinical classification of this disorder such as the following :—

1. Cysts not communicating with bronchi.
2. Cysts communicating with bronchi.
   (*a*) Simple unilocular cysts.
   (*b*) Multiple cysts (soap-bubble and berry types).

Congenital bronchial cysts which do not communicate with the bronchial tree are very rare, they contain fluid, and as far as is known produce no symptoms. In one case seen by the writer about sixteen such cysts varying in size from a pea to a golf ball were disclosed following the routine radiological examination of a patient aged forty. He had had no serious pulmonary disease and remained well during a five-year period of observation in which the radiological appearances persisted unchanged. Occasionally such a cyst may rupture into a bronchus, thereby discharging its contents, and subsequently behave as those of the second category.

Cysts communicating with bronchi contain air, and are characterised radiologically by very clearly defined thin limiting walls. As a rule they give rise to few distinctive signs or symptoms unless and until secondary infection supervenes. Occasionally, however, particularly in infants and children, increasing inflation of a solitary cyst by check-valve action of the communicating bronchus may occur and lead to gross increase in size of the cyst and all the consequences of a tension pneumothorax. Radiologically such cases may usually be differentiated from the latter by the absence of the collapsed lung at the hilum, and the presence of traces of pulmonary tissue at the periphery of the hemithorax. Furthermore, cysts communicating with bronchi are particularly liable to give rise to hæmoptysis, and when this happens the unexpectorated blood within the cyst sometimes clots. Under such circumstances a characteristic radiological picture is given ; for, with retraction of the clot from the cyst wall, the appearance of a stone loose within its setting is shown.

We do not know what is the proportion of cases of cystic disease of the

PLATE 23

Bronchogram of the right lung, showing basal bronchiectasis. (From film by Dr T. H. Hills.)

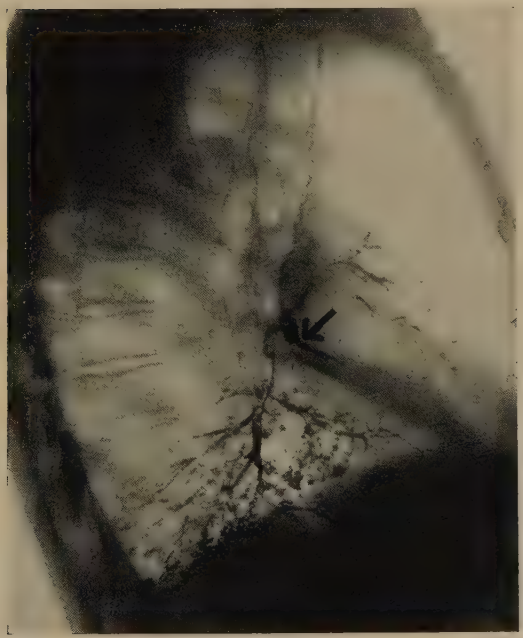

PLATE 24

Bronchial carcinoma (right lateral view). The middle lobe is collapsed and lipiodol shows obstruction, marked by an arrow. (From film by Dr T. H. Hills.)

[*To face page* 456.

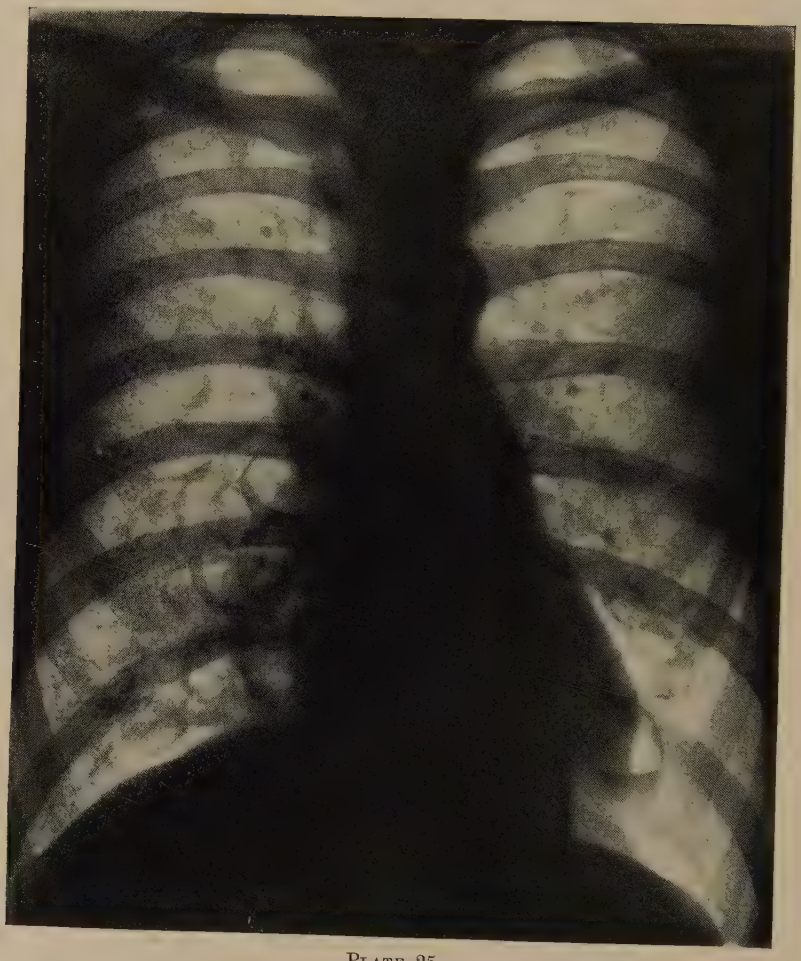

PLATE 25

Congenital cystic disease of the bronchi, with bilateral multiple air-filled cysts, some of which show fluid levels.

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lungs which remain uninfected throughout life, and since it is the advent of infection within the cyst or cysts which as a rule brings these cases to our notice, it is not improbable that at present we overestimate the probability of infection. In our own experience three cases, each over the age of fifty, have been encountered by chance in which there were and had been no symptoms associated with the disorder. On the other hand, septic infection when it does occur is commonly severe and often fatal. Attacks of bronchitis frequently accompanied by bronchial spasm may precede a fulminating septic pneumonia by months or even years. Large infected single cysts have the signs of and behave as would a lung abscess, while multiple cysts quickly give rise to the clinical syndrome of advanced bronchiectasis. When infection is sufficiently prolonged it is not unusual for acquired atelectasis and bronchiectasis to complicate the disorder. In such cases the clinical diagnosis of congenital cystic disease cannot be made with certainty.

In uninfected cases difficulty in diagnosis from localised pneumothorax and emphysematous bullæ may be encountered. The history of the case, the age of the patient, and the site, appearance, and shape of the lesion will be of assistance ; certainty of diagnosis, however, may only be obtained by histological examination after lobectomy.

Infected cysts have to be distinguished from empyema (including interlobar empyema), lung abscess, and saccular bronchiectasis. The failure to respond to adequate drainage will suggest a cyst rather than an empyema, while a lung abscess often shows clinical and radiological evidence of surrounding septic pneumonia. As has been said, it may not be possible to distinguish saccular bronchiectasis from cystic disease. The distinction, however, is of academic interest rather than of therapeutic importance.

Radical treatment of symptomless congenital cysts of the lung is rarely justified. Close observation and prophylactic measures designed to prevent respiratory infections are, however, necessary. The exceptions to this will as a rule be found among children in whom the chance of infection is relatively great, and whose resistance to the hazards of operation is considerable. Therapy in those cases with lesions productive of symptoms should, where possible, consist of radical removal by lobectomy or pneumonectomy, but adequate bronchography must precede the operation, for the disease is commonly bilateral or complicated by acquired bronchiectasis in the remaining pulmonary tissue. In acutely infected single cysts preliminary drainage may be of value.

In those cases in which suppuration has occurred and in which for any reason operative removal of the diseased area cannot be undertaken, postural drainage, expectorants, penicillin by inhalation or by intramuscular injection, and creosote may alleviate symptoms.

DISEASES OF THE LUNGS

Disorders of the Pulmonary Circulation

Hyperæmia.—Hyperæmia of the lungs accompanies all acute pulmonary and bronchial inflammatory diseases, and is seen most strikingly in acute broncho-pneumonia.

Pulmonary Hypertension.—Hypertension in the pulmonary circulation increases the work of the right ventricle, and in certain circumstances may

cause pulmonary heart disease. The process may be acute, or may occur gradually and be chronic. The most frequent cause of acute pulmonary hypertension is the sudden obstruction of a considerable proportion of the pulmonary circulation by embolism from a venous thrombus usually in the pelvis, abdomen, or leg, or from the right side of the heart itself. Only less abrupt is the vascular congestion which develops when left ventricular failure follows, for example, coronary infarction. As a consequence of the rise in pulmonary vascular pressure the lungs become less easily altered in shape, and respiration requires more effort. The intrapleural pressure fluctuates at a more nearly atmospheric level, and the chest can be seen to be relatively distended in expiration. The vital capacity is greatly reduced, while in addition pain may contribute to cause shallow respiration and so augment anoxæmia and a rapidly mounting cardiac distress.

Chronic pulmonary hypertension may arise in the course of many disorders. They fall into four groups: (i) obstruction of the pulmonary circulation within its own limits, *e.g.*, in emphysema and pulmonary fibrosis; (ii) obstruction of the pulmonary circulation outside its own limits, *e.g.*, in mitral stenosis; (iii) systemic-pulmonary vascular communications in certain types of congenital heart disease; (iv) severe kyphoscoliosis. Dyspnœa is the outstanding symptom. Cough, often productive, is frequently present, as is a minor degree of hæmoptysis. Cyanosis, clubbing, and polycythæmia are less constant and variable features.

Cardiac involvement is shown by enlargement of the conus arteriosus and right ventricle, with increased pulsation in the third and fourth left interspaces, an accentuated pulmonary second sound, and later gallop rhythm. When the right ventricle fails systemic venous engorgement, enlargement of the liver, œdema, ascites, oliguria, and sometimes nausea and vomiting occur. X-ray examination, apart from showing the cardiac changes and any pulmonary disease which may be present, demonstrates the distended pulmonary vessels spreading far out into the lungs.

Œdema of the Lungs.—Œdema of the lungs may result from infection, or the inhalation of irritant gases, but is commonly secondary to left ventricular failure, or renal disease; occasionally it develops after aspiration of a pleural effusion. The symptoms may come on suddenly; the patient is seized with extreme dyspnœa and pain in the chest, and expectorates large quantities of serous or blood-stained froth. He may lose consciousness and die, or the symptoms may subside after an hour or two and recovery take place; some patients have survived repeated attacks. Treatment is essentially that of left ventricular failure, and the most effective measures consist of rest, venesection, and the injection of $\frac{1}{4}$ gr. of morphia and $\frac{1}{100}$ gr. of atropine, followed by efficient oxygen administration.

Embolism and Infarction (*vide* p. 440).

EMPHYSEMA

In this condition the air sacs are dilated and their walls atrophied, while frequently the rupture of the walls of many alveoli results in the formation of bullæ. A number of varieties of the condition occur, the chief forms being known respectively as hypertrophic, atrophic, compensatory, acute vesicular, and acute interstitial.

Hypertrophic Emphysema.—*Ætiology.*—This is uncertain. Hypertrophic emphysema occurs frequently in some families, and may be associated with an inherent weakness of the elastic tissues of the lungs. Freund, on the other hand, has suggested that premature ossification of the costal cartilages, with immobility of the thoracic wall, is the primary change. The frequent occurrence of emphysema in association with bronchitis and asthma, however, would make it seem probable that long-continued respiratory obstruction is the important causal factor. Localised emphysema occurs when a bronchus is partially obstructed by, for example, a growth or stricture.

Morbid Anatomy.—The thorax is enlarged, chiefly in its anteroposterior diameter, and the intercostal spaces are wide. On opening the chest, the lungs fail to collapse; they are voluminous and hide the pericardium from view; they are pale in colour, and projecting bullæ may be seen, especially near the apices and anterior margins. Microscopic examination shows large, thin-walled alveoli, which in many places form extensive irregular chambers owing to disappearance of the inter-alveolar septa. These septa support the capillaries concerned in the gaseous exchanges of the blood, so that their disappearance causes a great diminution in the capillary bed of the pulmonary circulation. Sometimes enlargement of the conus and right ventricle may be found.

Symptoms.—The characteristic symptom of emphysema is dyspnœa. In the earlier stages this is only noticed on exertion, but as the condition develops the shortness of breath occurs with less provocation, until finally it is continuous even at rest, and may be accompanied by cyanosis and heart failure. The dyspnœa mainly results from the mechanical disadvantage of the increased residual air, from inadequate mixing of inspired and alveolar air, and from the decreased elasticity of the lungs. The symptoms are aggravated by the accompanying bronchitis, to which all emphysematous patients are susceptible.

Physical and Radiological Signs.—The condition is revealed by inspection of the thorax, which in characteristic cases is barrel-shaped. It is deep from back to front, the ribs are horizontal and kept in the position of inspiration, the subcostal angle is widened, and the normal 3 to 4 in. expansion is diminished to $1\frac{1}{2}$ in. or less. The shoulders are raised, the spine is kyphotic, and there is no visible impulse in the precordium. The percussion note is hyper-resonant, and dullness over the heart and liver is obliterated. The breath sounds are feeble and the expiratory murmur is prolonged. X-ray shows an enlarged thorax, horizontal widely spaced ribs, a low poorly moving diaphragm, and relatively more translucent lung fields. The heart is sometimes elongated and thin. In advanced cases pulmonary vascular engorgement with or without right ventricular hypertrophy may be seen. Large bullæ, crossed by fine strands of pulmonary tissue, are sometimes present, and may increase steadily in number and size.

Treatment.—The changes in the lungs are degenerative and irremediable. The chest wall may be rendered more mobile by suitable exercises, but the most profitable methods of treatment are those designed to cure or prevent bronchitis. Equable climatic conditions are of the greatest importance, and if possible the patient should not winter in a smoky city, or in a locality where sudden changes of temperature or cold winds are prevalent.

Atrophic Emphysema.—This is a senile change and accompanies other stigmata of degeneration. The alveolar walls become atrophic

and the septa give way, but the lungs are small and retracted and the ribs oblique.

Compensatory Emphysema.—This is a local distension of the alveoli, and is the result of shrinkage of other regions of the lungs from collapse or fibrosis. The intra-thoracic pressure being negative, when the contents of the chest become diminished by disease, the nearest healthy and elastic portions of the lungs become dilated to occupy the vacant space. At first the alveolar walls are simply stretched, but in course of time they become atrophied and true emphysema develops.

Acute Vesicular Emphysema.—This condition occurs as a result of sudden rupture of alveoli, such as may be associated with excessive cough and muscular strain. It is uncommon, but is found, for example, in cases of asphyxia, poisoning by irritant gases, whooping-cough, and acute laryngitis. Symptoms and signs are usually masked by those of the causal condition, but are essentially those given under hypertrophic emphysema.

Acute Interstitial Emphysema.—This is a variety of "surgical emphysema," in which air is driven through a rupture in the alveolar wall into the pulmonary interstitial tissues. It may occur in whooping-cough, as a result of trauma, blast injury, or muscular strain. If sufficiently extensive, it will involve the mediastinum and even spread to the neck and face. As a rule the air is absorbed spontaneously in a few days, though death may occur quickly. Clinically the patient is dyspnœic and may be cyanosed, and often complains of tightness and pain in the chest. Surgical emphysema may be palpable in the neck, crackling noises may be heard widely over the chest, and X-ray may show the presence of air in the soft tissues. Treatment consists of absolute rest, abolition of the cough reflex with morphia, and the administration of oxygen.

PULMONARY COLLAPSE

Collapse of the lung may be partial or complete. The former occurs when the diaphragm is elevated for any cause, or when, for example, air, or fluid of any kind accumulates in the pleural cavity. Both the air entry and the blood and lymph flow in the involved lung are diminished in proportion to the extent of the collapse, while a compensatory increase in ventilation and circulation takes place in the other lung. The diminution in air entry is reflected in the physical signs which are otherwise those of the causal condition. Radiological examination reveals the cause and indicates the extent of the collapse. As a rule re-expansion of the lung from partial collapse immediately or rapidly follows the removal of the productive lesion, and there are then no pulmonary sequelæ. Complete collapse of lung, often called pulmonary atelectasis, may persist because the lung does not expand at birth, or may develop following absorption of air by the circulating blood if a bronchus or bronchiole is completely obstructed. The causes of such an obstruction have been discussed (*vide* p. 449).

Acquired pulmonary atelectasis is a common condition. It plays a fundamental part in the pathology of many pulmonary inflammations and injuries, is frequently associated with any kind of intrathoracic tumour, and may supervene upon partial pulmonary collapse from kinking or defective drainage of a bronchus. The extent of the lesion is determined by the size and

number of bronchi or bronchioles obstructed ; thus, a lobe or the whole lung becomes atelectatic respectively if the lobar or main bronchus is occluded (the so-called massive collapse), while scattered lobular atelectasis follows multiple bronchiolar obstruction. The lower lobes are most commonly affected, and the left lower lobe more commonly than the right.

Complete collapse of an area of lung diminishes the volume of the thoracic contents. Partial compensation occurs by displacement of the thoracic parietes and mediastinum towards the collapsed area, by emphysema of the remaining and particularly the adjacent pulmonary tissue, and by dilatation of bronchi and blood vessels within the atelectatic lung. Since of these structures some are semi-rigid, some relatively elastic, the change occurs at the expense of the development of an increase of tension locally—a measure of which may be obtained if the intrapleural pressure is recorded, when it will be found that this pressure is more removed from atmospheric (more negative) than is the case over normal lung. Important changes follow. Vascular dilatation within the completely collapsed lung has as a result the return of venous blood to the left side of the heart, and, therefore, a fall in the oxygen saturation of the arterial blood. Further impairment of circulatory function is due to the distortion of the great veins arising from mediastinal displacement, and this effect is enhanced as may be shown at radioscopy with each inspiration.

Emphysema of adjacent lung may become permanent, and similarly the stretched bronchi may lose their elasticity beyond recovery particularly if infection of their muscle coats supervenes. Since with bronchial obstruction the drainage of the sputum ceases, infection in these bronchi and in the collapsed lung as a rule quickly follows. Bronchiectasis, and pulmonary suppuration with lung abscess formation, may therefore develop. Pulmonary atelectasis may persist even if the cause is removed.

Symptoms.—Congenital pulmonary atelectasis causes pallid asphyxia. The acquired form, if extensive, gives rise to cough, dyspnœa, cyanosis, and pleuritic pain from the onset of collapse, while to these are added the consequences of infection if and when that occurs.

Physical and Radiological Signs.—Diminution in size and limitation of the movement of the chest wall on the affected side may be seen and felt, as may displacement of the heart and trachea. Over the atelectatic lung the percussion note is impaired, while adjacent areas will be hyper-resonant. Atelectatic lung conducts sound at least as well as does consolidated lung ; when, therefore, it is adjacent to a bronchus through which air is passing, auscultation will reveal bronchial breathing, bronchophony, and whispering pectoriloquy, though when the atelectatic area (*e.g.*, a lower lobe) is distant from such a bronchus breath sounds and vocal resonance may be diminished or absent.

Radiologically atelectatic lung is homogeneously opaque. The site and size of the opacity will depend upon the area of lung involved, and there will in addition be associated emphysema of adjacent lung, and mediastinal displacement towards the affected area. Multilobular atelectasis can only be differentiated radiologically from broncho-pneumonia by this displacement.

Treatment.—The treatment of partial pulmonary collapse is that of the cause. Pulmonary atelectasis arising as a result of the inhalation of foreign bodies, or by viscid sputum, or blood clot obstructing a major bronchus is a medical emergency which may demand bronchoscopy when the obstruction

can frequently be removed. This procedure may also permit accurate diagnosis in those cases in which the cause is not obvious by routine investigation. In multilobular atelectasis and in cases where bronchoscopy fails to relieve the atelectasis, and where no gross cause such as neoplastic disease is present, postural drainage, an expectorant containing potassium iodide, inhalations of 5 per cent. CO_2 in oxygen, and breathing exercises may be advisable. Some of the serious consequences of extensive temporary atelectasis may be prevented by the induction and maintenance of a small pneumothorax until bronchial obstruction is relieved. The treatment of intrathoracic tumours, and of the bronchiectasis and other consequences arising from pulmonary atelectasis is set forth elsewhere.

THE PNEUMONIAS

Pneumonia is essentially an inflammation of the substance of the lung, with the production of exudate in the alveoli. Classically two main types are recognised : (i) lobar or croupous pneumonia and (ii) lobular or broncho-pneumonia. Lobar pneumonia is a specific infective disease with a characteristic clinical course, due to a particular organism.

Broncho-pneumonia is in most instances a secondary condition ; its course is indefinite and bacteriology variable, and it is possible to distinguish several varieties which have fairly well-defined clinical and pathological characteristics.

In addition there exists an ill-defined group of non-specific pulmonary inflammations, some relatively benign and of short duration, others much more chronic, which are at present best classified among the pneumonias.

LOBAR PNEUMONIA

Bacteriology.—The causative organism in more than 90 per cent. of cases is the pneumococcus. This is a capsulated lanceolate gram-positive coccus growing in pairs or short chains. Investigation of pneumococci derived from cases of lobar pneumonia permits their separation into three main types and a fourth group consisting of many which give slightly differing serological reactions. Sera which have a limited value can be prepared and used therapeutically against types one and two. Streptococci, staphylococci, Friedländer's bacillus, and rarely other organisms may cause lobar pneumonia.

Ætiology.—Lobar pneumonia occurs most commonly in temperate climates, and it accounts for a greater number of deaths than any other acute disease in the United Kingdom. Although most cases are sporadic, widespread epidemics occur from time to time. It is common at the two extremes of life, and relatively rare between the ages of six and fifteen years. In children complications such as empyema are frequent, but the mortality is low ; after the thirtieth year mortality rises with each decade. In children the sexes are attacked equally, but in adults 70 per cent. of cases occur in males. One attack does not confer immunity ; on the contrary, one or more recurrences often follow, and Rush has recorded a case in which one individual had pneumonia

twenty-eight times. Successive attacks are usually mild. The negro races are specially susceptible.

Pneumonia sometimes follows chest injuries and the inhalation of irritant gases, but the commonest ætiological factors are those which impair the defensive mechanism against infections, such as poverty, malnutrition, exhaustion, old age, and chronic debilitating diseases. Instances of the latter are diabetes, nephritis, portal cirrhosis, and chronic alcoholism ; moreover it is said that one-sixth of all insane persons die of pneumonia (G. W. Norris). Of acute illnesses influenza is the one most often complicated by pneumococcal pneumonia, though it usually takes the lobular form. When healthy young adults are attacked it may be a result of exposure to cold, or exhaustion following violent physical exertion. Lobar pneumonia occasionally follows operations, though post-operative complications such as broncho-pneumonia, massive collapse, or infarction are more common.

As a result of chemotherapy the mortality of pneumonia has greatly decreased even among the aged, who now often survive what ten years ago would have been an almost invariably fatal illness.

Pathology and Morbid Anatomy.—The disease may begin as a septicæmia. Pneumococci may often be demonstrated in the blood stream in the first few days of a severe infection. Inhalation, however, is probably the usual method of infection, and the specific organism can usually soon be recovered from the sputum. The inflammatory reaction in the lungs passes through four stages, and pneumococci can be demonstrated to be present in the affected area during the earlier of these. The first is the stage of *congestion* ; the affected portion of the lung is dark red and heavy, though it still contains sufficient air to float in water. The capillaries are dilated, and the alveoli contain a little fluid resembling blood. The second stage is that of *red hepatisation*, the lung resembling liver in appearance and consistency. The affected lobe is swollen and of a reddish-brown colour, the pleura is dull and covered with a film of yellow fibrin. The air sacs are filled with solid fibrinous clot in which are entangled many red cells and some leucocytes. The lung tissue is friable, and so heavy that it sinks when placed in water. The third stage is that of *grey hepatisation* ; the consistency is similar to that of the second stage, but the colour is changed to a reddish-grey. The size of the affected lobe is further increased, the pleura is covered with thick yellow exudate, and an ounce or two of turbid fluid may be seen in the pleural cavity. Microscopically the clot in the air sacs is found to be crowded with leucocytes. The red cells are degenerate and leucocytes contain numerous fat droplets. In the stage of *resolution* the appearance resembles that of grey hepatisation, but has a remarkable translucency. Inflammatory blood-borne lesions may be found in other organs : pericarditis often accompanies left-sided pneumonia, and acute bacterial endocarditis, arthritis, and meningitis are sometimes seen ; colitis also occurs.

The right lung is attacked more often than the left, and the lower lobe is usually the one first affected. The inflammation may spread to a contiguous lobe, or to a lobe of the opposite lung.

Symptoms.—The onset is sudden, often with a rigor, and the temperature rises to 103° F. or over on the first day. In children the onset is commonly indicated by vomiting and sometimes by meningism. The pyrexia is continuous and lasts from five to nine days, then falls suddenly to normal in a few hours ; at the same time pulse and respiration rates fall, and the whole aspect of the

patient changes from one of great distress to one of comfort. This abrupt termination is known as the *crisis*. In more than one-third of the cases the symptoms subside gradually and the temperature takes several days to reach the normal level—termination by *lysis*. At the onset the patient complains of an agonising pain in the side, due to accompanying pleurisy. If diaphragmatic pleurisy is present, pain may be referred to the abdomen or to the tip of the shoulder. There is a dry painful cough and tenacious mucoid sputum. The patient lies on the affected side, his face is flushed, often on one cheek only, labial herpes often appears about the third day, the tongue is coated, and the skin dry. Breathing is rapid and jerky with an expiratory grunt, and the *alæ nasi* dilate with each breath. Although there is tachycardia the respiration rate is usually proportionately more increased so that the pulse respiration ratio falls to 3 : 1 or even 2 : 1. Sometimes hæmolytic jaundice develops. The sputum is usually mucoid at first ; after twenty-four hours it becomes blood-stained, and later the bright red changes to a pale rust colour. Nocturnal delirium is apt to occur, especially when the upper lobe is affected, and is frequent in alcoholics. Constipation, anorexia, and loss of weight are common.

The extending use of penicillin and the sulphonamides in cases of lobar pneumonia has already so modified the course of the disease that classical cases as described above with continued fever and a crisis are already uncommon, and may well soon become rare. The majority react to chemotherapy within forty-eight hours and the temperature chart then shows no characteristic form.

Physical and Radiological Signs.—On inspection of the chest the affected side usually moves less than the other, but the difference may not be great. In the stage of congestion the only abnormal sign may be slight impairment of resonance, but fine râles are often audible, especially after cough. In the stages of red and grey hepatisation there is dullness to percussion over an area roughly corresponding with a lobe of the lung, and auscultation reveals tubular breathing which becomes extremely striking when the consolidation is complete. A pleural rub is commonly audible. Together with this alteration of the breath sounds, bronchophony and pectoriloquy are heard. These physical signs appear about the fourth day, and some days after the crisis as resolution of the inflammatory exudate takes place coarse râles (redux crepitations) appear over the affected area, and the signs of consolidation become patchy and disappear.

Typically, X-ray shows a more or less uniform opacity corresponding in size and position to the affected lobe. With resolution this area becomes increasingly mottled by re-aerated lung.

Examination of the blood shows a great increase in the number of leucocytes, which may number from 20,000 to 60,000 per cubic millimetre. This increase, which is mainly made up of polymorphonuclear cells, is found in the earliest stage of the disease and subsides with the crisis. The white count is of considerable value in estimating the prognosis ; a white count of less than 10,000 indicates a very poor chance of recovery.

The urine is scanty and highly coloured, there is a retention of chlorides in the body, and a diminution of these salts in the urine until after the crisis. Albuminuria is constant, while hyaline and granular casts are commonly found. These abnormalities are usually due to toxic nephrosis, which is often minor in degree.

Complications.—Lobar pneumonia is often free from complications, and many will be prevented or be best treated by early effective chemotherapy. The following occur :—

1. *Pleurisy* occurs regularly, and quite often (particularly if chemotherapy has been employed) is followed by effusion. Empyema is not infrequent (*vide* p. 494).

2. *Pericarditis.*—This does not differ from other forms of acute pericarditis as regards signs and symptoms. The exudate is thick and " buttery " and of a yellow or slightly green colour. This complication is most often seen in left-sided pneumonia. Surgical drainage may be advisable as in empyema.

3. *Endocarditis.*—This rare complication, which may cause a second rigor, is found occasionally at autopsy and affects particularly the aortic valve. It has in the past always been fatal.

4. *Circulatory Failure.*—Peripheral circulatory failure is not uncommon, while occasionally congestive heart failure complicates the disease.

5. *Meningitis.*—Pneumococcal meningitis usually occurs without involvement of the lungs. It can be distinguished from other forms of acute meningitis only by bacteriological examination of the cerebrospinal fluid. It is often fatal. It must be distinguished from the meningism sometimes occurring especially in children in the septicæmic stage of pneumonia, in which there may be neck rigidity and Kernig's sign, but the cerebrospinal fluid is normal.

6. *Peritonitis* (*vide* p. 362).

7. *Otitis Media.*—This may be a complication of pneumonia or may arise independently. The treatment is surgical. When bilateral mastoid disease occurs the condition is almost invariably fatal.

8. *Arthritis.*—The pneumococcus occasionally produces an acute suppurative arthritis involving one of the larger joints. Aspiration of the pus should be tried before having recourse to open operation.

Colitis, nephritis, phlebitis with venous thrombosis, parotitis, peripheral neuritis, and hæmolytic jaundice may occur. Very rarely the lung tissue may break down to form an abscess, or extensive necrosis give rise to gangrene. Occasionally the exudate in the alveoli fails to liquefy, resolution does not take place, and there is an invasion of connective tissue cells which produce a network of fibrous tissue—unresolved pneumonia. Minor degrees of this organisation, resulting in fibrosis, are quite common. Bronchial obstruction by debris during resolution may lead to atelectasis of the area of lung concerned. Numerous cases are met with in which a lobar pneumonia is followed after an interval by recurring attacks of bronchitis or by spasmodic asthma. A proportion of such cases are associated with a secondary bronchiectasis.

Prognosis.—In children death rarely results from uncomplicated lobar pneumonia. In adults, as has already been pointed out, the prognosis becomes increasingly grave after the fortieth year, and in the aged the disease is frequently fatal. A robust physique has little influence on the course of the disease, but, on the other hand, the temperament of the patient is of great importance. Optimism and a determination to survive are of great assistance, whereas alarm and despondency may defeat efforts at treatment. Other unfavourable features are alcoholism and chronic diseases, such as diabetes or nephritis.

Though it is always difficult to forecast the course of any individual case, there are, however, certain unfavourable indications. Among these are : a

very high temperature, or, on the other hand, a practically apyrexial course, such as occurs in feeble and elderly subjects ; severe toxæmia with delirium or cyanosis, especially when appearing early ; involvement of several lobes in one or both lungs. In addition, a positive blood culture indicates massive infection, while a low leucocyte count implies a failure of protective reaction. Failure to respond to chemotherapy adds greatly to the gravity of the prognosis.

Diagnosis.—Difficulty sometimes arises in distinguishing lobar pneumonia from pleural effusion, atelectasis, pulmonary infarction, broncho-pneumonia, acute tuberculous pneumonia, and acute septic peritonitis.

Apart from the symptoms in pleural effusion, the distinguishing features are the shape of the area of impaired resonance, the obliteration of tactile vocal fremitus, and the displacement of the heart and trachea away from the affected side of the chest ; an exploratory puncture of the pleura will settle the question. In massive collapse or atelectasis the diagnostic sign is displacement of the heart and trachea *towards* the dull area in the lung. The radiological appearances in pleural effusion and massive collapse are quite characteristic (*vide* pp. 488 and 461 respectively). Infarction is met with most frequently about ten days after a surgical operation, the onset is abrupt and painful, and is followed in a few hours by expectoration of frankly blood-stained material, quite different from the rusty sputum which appears some days after the onset of a lobar pneumonia. Broncho-pneumonia is nearly always bilateral, shows from the first patchy mottled shadows on X-ray examination, and except in its primary form is characterised by a very different temperature range and clinical aspect from lobar pneumonia. Acute tuberculous pneumonia may at first be indistinguishable from the pneumococcal form, but its long duration will give rise to suspicion, and a bacteriological examination of the sputum will reveal its true nature. Acute pneumonia of one of the lower lobes, with diaphragmatic pleurisy, may give rise to severe abdominal pain with vomiting and constipation, and present a clinical picture closely resembling that of appendicitis or other acute peritoneal inflammation. Many such patients have been subjected to an unnecessary laparotomy with dire results. The increased respiration rate is suggestive of pneumonia, while a careful clinical and X-ray examination of the chest will usually prevent this error.

Treatment.—Important measures are to ensure abundant fresh air and complete rest. The patient is propped up in a comfortable position in bed and must be disturbed as little as possible. Efficient nursing is essential, and both day and night nurses are necessities.

Chemotherapy has vastly improved the outlook in all cases of lobar pneumonia. Sulphamezathine or other appropriate drug may be given. For an adult it may be given by mouth as follows : 4 gm., then in six hours 3 gm., then 2 gm. six-hourly until sixty hours is reached. Details regarding the administration of sulphonamide drugs are given on page 7. In infants and young children 0·2 gm. per kilo. body-weight daily of sulphamezathine in suitably divided doses is satisfactory. In severe infections, when the prognosis is poor, or when the infection proves resistant to these drugs, penicillin should be used as follows : 100,000 units by inhalation with a Collinson inhaler, or intramuscular injection four-hourly in the day, while in the evening a final injection of 200,000 units is given. The patient is allowed to sleep through the night undisturbed. Therapy should be continued in this

way for two days after marked clinical improvement and a return of the temperature to normal has occurred.

With cyanosis and respiratory distress continuous inhalation of oxygen is most valuable; it may be bubbled through water in a flow-meter, and administered through a mask, bilateral nasal catheters, or the patient may be placed in an oxygen tent. The rate of administration should be adjusted so that a concentration of oxygen of more than 40 per cent. is maintained in the alveoli.

Circulatory and cardiac failure may occur. They are usually encountered after the fifth day of the illness, and on this account many physicians administer digitalis by mouth from the commencement, but its value is doubtful. Repeated hypodermic injection of so-called cardiac tonics, such as strychnine or camphor, are to be deprecated. Alcohol in the form of brandy or champagne is of use to allay anxiety and induce sleep; in alcoholics it is essential for the prevention of delirium tremens. Abdominal distension may be a distressing feature, adding to the respiratory embarrassment. It must be relieved by turpentine enemata, followed, if necessary, by intramuscular injections of pituitrin or eserine.

Insomnia is one of the most dangerous symptoms, and must be prevented at all costs. Chloral, bromide, or Dover's powder should be tried, but if they prove ineffective an injection of morphia or 100 mg. of pethedine should be used.

Pain due to pleurisy may be relieved by local applications, such as antiphlogistine, an electrically heated pad, and by strapping the affected side of the chest, or, if necessary, by inducing a small pneumothorax. Unproductive cough is best treated with a linctus (syr. codeinæ, syr. pruni Virg. aa ℥ii, p.r.n.), while an alkaline expectorant containing potassium iodide (pot. iod. gr. iii, ammon. carb. gr. iii, tinct. scillæ ℥xx, aq. chloroformi ad ℥ss) or steam inhalations render the expectoration of sputum, otherwise thick and viscid, an easier matter.

Pyrexia is part of the protective reaction and should not be treated unless dangerously high, and antipyretics are never beneficial. A temperature of 104·5° F. or over indicates the need for tepid sponging.

An abundance of fluid containing glucose should be taken, and sufficient light food in the form of milk, jellies, and fruit juice with sugar to maintain nutrition. Laxatives are given to aid elimination. The possibility of the patient getting out of bed and throwing himself from a window while delirious must be guarded against.

The patient should be trained in and should frequently practise for several months exercises to restore full mobility and expansion in the lung. These exercises are of the greatest importance in children. If carried out as a routine, the incidence of sequelæ such as bronchitis and bronchiectasis would be considerably reduced.

Ample time should be allowed for convalescence, and work should not be resumed for about two months after the crisis.

A correspondingly shorter period will suffice in cases when the disease has been successfully aborted by chemotherapy.

Varieties of Lobar Pneumonia

Study of the variations in the clinical course of lobar pneumonia have suggested that the various types of pneumococci tend constantly to give rise

to fairly characteristic disease forms. Further investigation is, however, necessary before these can be distinguished with any certainty.

Apical Pneumonia, by which is meant involvement of an upper lobe, is seen most commonly in children, in whom it is no more dangerous than other forms. In adults this variety is said to occur with special frequency in alcoholics and to be associated with delirium and a high fatality. In children epituberculosis, in young adults pulmonary tuberculosis, and in the middle-aged and old bronchial carcinoma may cause difficulty in diagnosis.

Senile or Asthenic Pneumonia occurs in debilitated subjects. There may be no pyrexia nor any of the usual symptoms, and the outlook is serious.

Pneumonia in Children is usually characterised by an abrupt onset with convulsions or vomiting. The course is only three to five days as a rule, and there is little danger to life unless complications occur. Empyema and middle-ear disease are, however, much commoner than in adults. Empyema develops most commonly between the tenth and twentieth day, but in cases developing before the seventh day the mortality is high.

BRONCHO-PNEUMONIA (*Lobular Pneumonia*)

Ætiology.—Broncho-pneumonia is not a specific disease, but is an inclusive term for a variety of conditions characterised by scattered areas of inflammation in the lungs.

Primary Broncho-pneumonia is seen only in children under three years of age, and is due to infection with the pneumococcus. The symptoms and course are the same as those of pneumococcal lobar pneumonia.

Secondary Broncho-pneumonia may occur at any age and affects both sexes equally. It is due to infection with a variety of organisms, several of which may usually be found in the affected areas of the lungs. The pneumococcus *Streptococcus hæmolyticus*, *Staphylococcus aureus*, *B. influenzæ*, and *B. friedlanderi* are the most common. Tuberculous broncho-pneumonia has been described elsewhere (*vide* p. 92). The infection characteristically descends to the terminal branches and air sacs from the upper respiratory tract; it is a common complication of the infectious fevers such as measles, whooping-cough, diphtheria, typhoid, influenza, erysipelas, and smallpox. "Aspiration broncho-pneumonia" results from septic material being drawn into the bronchioles by the respiratory movements. This material may come from infected cavities within the lungs, for example, lung abscess, or bronchiectasis; from adjacent collections of pus such as liver or subphrenic abscess which may rupture into the lung; it may come from the mouth or throat, especially during operations under a general anæsthetic; it may follow vomiting while in a state of insensibility, and it is a common sequel in those rescued from drowning. Like lobar pneumonia, it often terminates a long illness such as diabetes or nephritis in debilitated subjects.

Pathology and Morbid Anatomy.—There is reason to believe that local atelectasis, caused by the plugging of small bronchioles with infected material, is a frequent, if not an invariable, precursor of broncho-pneumonia. The lesions are bilateral in 82 per cent. of cases (Holt), and the parts most commonly affected are the posterior portions of the lower lobes; small effusions into the pleural sacs are by no means rare. On the surface of the lungs are seen blue depressed atelectatic areas which are separated from one

another by areas of compensatory emphysema, and there is roughening of the pleura over the more superficial areas of consolidation. The latter are felt as firm nodules when the lungs are handled, and on section the consolidated areas project above the cut surface. They vary in colour and size ; the more recent are dark red and the older are grey or yellow. The lesions are grouped round a small bronchus which is filled with pus, the air sacs are filled with exudate, and beyond these are areas of congestion and of atelectasis. In severe cases a focus may necrose with formation of an abscess, or wide areas of lung tissue may become gangrenous, but in milder cases ending in recovery the inflammatory changes may subside and leave no permanent alteration of structure. Organisation of the exudate, with formation of fibrous tissue, persistent atelectasis, and ultimately bronchiectasis occurs most commonly in children.

Symptoms.—The onset is usually insidious, but after a few days the toxæmia is severe, with languor, tachycardia, dyspnœa, and cyanosis. The temperature rises gradually and is very irregular, usually higher in the evening than the morning, and varying from day to day ; there may be no pyrexia at all, even in cases terminating fatally. Pain is seldom severe and it may be absent, but there is often restlessness and distress, while the respirations are shallow and sometimes as rapid as fifty a minute. The sputum is muco-purulent ; it is sometimes streaked with blood, and free hæmoptysis is seen in the influenzal form, but rusty sputum like that of lobar pneumonia does not occur. Drowsiness and delirium are common in cases showing lividity. The disease runs an irregular course, lasting from two to five weeks. Death results from exhaustion, anoxæmia, or cardiac failure, but at any stage the symptoms may subside and recovery take place. Secondary broncho-pneumonia has a high mortality. Complications, except heart failure, are not frequent, but sequelæ in the shape of fibrosis and bronchiectasis are common.

Physical and Radiological Signs.—In the early stages signs of consolidation are usually absent, but there may be obvious evidence of bronchitis. Cyanosis is common. After a few days, careful auscultation of the lower lobes will generally reveal limited areas of tubular breathing with pectoriloquy and fine crackling râles. If the lesions become confluent, extensive signs of consolidation may be obtained. X-ray examination shows multiple variously sized scattered shadows throughout the lungs, concentrated commonly in the lower zones. Many of these may become confluent and so form an area of consolidation ; in such areas resolution is relatively slow. Coexistent atelectasis may be seen.

Prognosis.—Primary (pneumococcal) broncho-pneumonia is frequently fatal in infants, but in children it runs a short course and recovery is the rule. Secondary broncho-pneumonia has a more prolonged course, and it must always be regarded as a dangerous condition, especially at the two extremes of life. Restlessness, lividity, a pulse rate higher than 130 in an adult, and a low blood pressure are signs of grave import.

Treatment.—Treatment is carried out on the same lines as in lobar pneumonia. If on bacteriological examination the infecting organism proves to be one which is sensitive to chemotherapy this method should be used in the way described for lobar pneumonia. The dosage of penicillin is also similar. Either of these methods of treatment may be begun while awaiting bacteriological evidence. As the fever may last several weeks, special

attention must be paid to nutrition, and frequent feeds should be given. The diet consists of milk with prepared cereals, or beaten eggs, jellies, and abundance of sugar. The early administration of expectorants, together with frequent periods of inhalation of oxygen containing 7 per cent. carbon dioxide, may shorten the disease by preventing the spread of lobular atelectasis. Oxygen therapy is very important. It should be given by mask or tent for long periods, and, if possible, in sufficient amounts to relieve cyanosis and dyspnœa. Consecutive heart failure needs energetic treatment.

Breathing exercises from a very early stage may also diminish further development of the infection and if continued may prevent bronchiectasis.

UNRESOLVED PNEUMONIA

In most cases of acute lobar pneumonia the exudate in the alveoli becomes completely liquefied before the tenth day and the lung soon recovers its normal consistency and function. In a few cases, however, this sudden change does not occur, especially when bronchial obstruction and atelectasis complicate the infection. The persisting exudate becomes invaded by blood vessels and connective-tissue cells, so that in course of time a network of fibrous tissue is formed in the affected lobe, which becomes shrunken, pale, and tough. Infecting organisms breed in the stagnant bronchial secretions, and the walls of the tubes become softened and dilated. Pneumococci are found in the lung, but these are seldom in pure culture, and there is usually a mixed infection with the influenza bacillus or the *Streptococcus viridans*.

Confluent broncho-pneumonia even more commonly fails to resolve and so gives rise to fibroid change in the lungs ; in such cases the process is more diffuse and affects areas in the lower portions of both lungs. It has seemed probable to many observers that unresolved pneumonia has occurred more commonly since chemotherapy has been in general use for pneumonia.

Symptoms.—Following an attack of broncho- or lobar pneumonia the patient fails to improve. The pyrexia seldom exceeds 102° or 103° F., but it persists for several weeks and sometimes for months. There is cough, blood-stained or purulent sputum, pain in the side, and dyspnœa, but the toxæmia is usually less profound than that of acute pneumonia. The pyrexia subsides gradually, and the patient is able to resume his occupation, but there is permanent limitation of his capacity for exercise, cyanosis, dyspnœa, and a persistent productive cough. As the fibroid change develops he becomes subject to recurrent attacks of bronchitis, and in some cases to spasmodic asthma, while bronchiectatic change is shown by purulent sputum and hæmoptysis. In the presence of secondary bronchiectasis the lung may be the seat of repeated attacks or relapses of pneumonic consolidation, which may recur every few months for many years, each attack being accompanied by toxæmia and pyrexia, lasting from six to ten days.

Physical and Radiological Signs.—During the stage of consolidation, the physical signs may be indistinguishable from those of acute pneumonia, with dullness, tubular breathing, bronchophony, and pectoriloquy over an area corresponding to one of the lower lobes. In most cases, however, there is dullness corresponding to the affected area, while breath and voice sounds are greatly diminished in intensity. As the consolidation clears and is replaced by fibroid change, new physical signs appear. The fingers become clubbed, the

affected side of the chest immobile, the intercostal spaces narrowed; the vertebral column is curved laterally with its concavity towards the affected side, and the heart is displaced towards the fibroid lung. Percussion reveals less impairment of resonance, the breath sounds, in the absence of bronchiectasis, may be of normal character though less loud than over the normal lung, and numerous moist râles are heard over the fibrotic lobe. If a relapse of the pneumonic inflammation occurs, the affected lobe may again give rise to signs of consolidation, though more frequently dullness to percussion, limitation of movement and air entry, and diminished voice sounds are encountered.

Variable X-ray appearances are seen. Commonly with consolidation an irregular opacity of fluctuating density is found associated with outlying ill-defined smaller shadows. Mediastinal structures are commonly displaced towards, the lesion and the pleura is generally markedly thickened.

Diagnosis.—In the stage of consolidation, pleural effusion is often suspected; but the signs differ in that the cardiac impulse is not displaced away from the affected side, the dull area corresponds in shape to a lobe of the lung, and does not have the oblique upper limit sloping downwards from axilla to vertebral column which is typical of effusion; moreover, tactile fremitus is not completely abolished. In the relapsing type, clubbing of the fingers with tachycardia, dyspnœa on exertion, and bouts of pyrexia may lead to a mistaken diagnosis of infective endocarditis, but careful examination of the chest and recognition of the characteristic short periods of pyrexia should prevent confusion. Bronchial carcinoma may cause exactly this sequence of events so that bronchoscopy may be needed in diagnosis. Pulmonary tuberculosis more commonly involves the upper lobes, has as a rule a different X-ray appearance, and if active will sooner or later give rise to sputum containing tubercle bacilli.

Prognosis.—The disease is not often fatal but it leads to permanent impairment of health unless treatment is intelligent and persevering. Profound toxæmia, especially if accompanied by mental disturbance, is an indication of danger. The longer resolution is delayed the more probably will bronchiectasis result.

Treatment.—Bronchoscopy should be performed as soon as it becomes apparent that bronchial obstruction has complicated the course of pneumonia. The above-mentioned signs or undue delay in resolution will suggest this. If the obstructing plug of debris can be found it should be removed by suction. The infecting organism should be tested for its resistance to the sulphonamides or penicillin. If it is not resistant a further course of chemotherapy may successfully overcome the infection. Great benefit is derived from remedial exercises designed to distend and restore mobility to the affected lobe. The exercises should be commenced at a very early stage and before fibrotic changes have become established; but even years later it may be possible to achieve some measure of success. The treatment must be carried out frequently, and practised assiduously several times daily in some cases for years. Distension of the affected lung is obtained by deep breathing while the sound side of the thorax is immobilised. The patient lies on the healthy side with the hip and shoulder supported on a low couch and a hard bolster under the lower ribs. His legs are unsupported and the feet rest on the floor, while he steadies himself by grasping a support with the uppermost arm extended over his head. He then takes a series of slow deep breaths. and with each

inspiration an assistant lifts him clear of the couch by hands placed under the lower part of the chest. Thus during inspiration the patient's weight is thrown on the sound side of his chest, and he is in such a position that the ribs of the healthy side are crowded together and fixed, but the opposite chest wall is expanded. An adjunct to the treatment is the inhalation of steam and tinct. benz. Co. (℥i to a pint of nearly boiling water). Autogenous vaccines are often administered but in the writer's experience have had no effect.

Other Varieties of Pneumonia

Pneumonitis.—The use of this term, which means inflammation of the lung, has grown during the last decade. A heterogeneous group of conditions are covered, including those discussed above and in this section, pulmonary suppuration in addition to multilobular atelectasis, and a variety of specific infections of the lung. In view of the absence of a precise meaning the term is best avoided.

Fat Embolism (*vide* p. 492).

Septic Infarcts.—Following operation, or associated with septic thrombophlebitis, or pyæmia, multiple infarcts may occur throughout the lungs and these may each lead to necrosis and abscess formation. A variety of organisms may be concerned, particularly the staphylococcus. The condition at first resembles an acute broncho-pneumonia, later its more severe course, the increasing volume of purulent sputum, and the radiological appearance of multiple abscess cavities are fairly characteristic, while the causal factor may be obvious. Penicillin therapy is essential from an early stage.

Primary Atypical Pneumonia.—This relatively benign disorder which predominantly affects young adults, and occurs sporadically and in epidemics, is now recognised as a distinct entity. The onset is insidious, and malaise, headache, shivering, and an irritating cough are features. The fever is moderate, and subsides by lysis in about a week. Only minor physical signs are as a rule present over the chest, though slight pharyngitis is often present. Purulent sputum may be produced after some days, and then râles and rhonchi can be heard. The ætiology and pathology are uncertain, but chemotherapy is of no value. Pleurisy, herpes, hæmoptysis, dyspnœa, tachycardia, and leucocytosis are usually absent. X-ray shows as a rule diffuse mottling in one or both lower lobes. Therapy is that of bronchitis. The disease is rarely fatal and is strikingly free from complications.

Chronic Pneumonia.—Not infrequently from the onset, which is insidious, pneumonia may be chronic. Variability is considerable; thus, in the less chronic forms progression to lung abscess takes place fairly quickly, in others this may occur after a long period of very slight toxæmia. In some cases, called chronic diffuse broncho-pneumonia by Scadding, a fairly characteristic clinical course occurred usually with a fatal outcome. The nature of the infection is inconstant, and several organisms may be concerned. Increasing dyspnœa, cough with purulent and sometimes blood-stained sputum, irregular, recurrent, or persistent pyrexia and toxæmia are important features, as are pleuritic pain, sweating, anorexia, and loss of weight. Tuberculosis, bronchiectasis, bronchial neoplasm, actinomycosis, and syphilis of the lung may be with difficulty excluded. Therapy is that of unresolved pneumonia.

Other Pneumonias.—Various forms of acute and chronic pneumonia may be encountered in upper respiratory infections, influenza, psittacosis and other virus infections, enteric fever, plague, and other zymotic diseases.

PULMONARY ABSCESS AND GANGRENE

Ætiology.—The two usual causes of lung abscess are : (i) aspiration of a foreign body or infected material into the bronchi ; and (ii) the suppuration of a pneumonic area, which is much less common in lobar than in broncho-pneumonia. Other and less frequent causes are chronic pneumonia, septic emboli, bronchiectasis, bronchial carcinoma or stricture, rupture of an empyema or subphrenic abscess, wounds of the lung, perforation of the œsophagus, and liver abscess.

The above conditions may also cause gangrene of the lung in cases in which the toxæmia is overwhelming.

Aspiration abscesses are mostly seen after operations on the nose and throat, such as tonsillectomy, and after the extraction of teeth. Experimentally a lung abscess can only be produced by the combination of bacterial embolism and bronchial obstruction.

Morbid Anatomy.—A recent abscess appears as an irregular cavity with ragged walls, containing sloughs of foul-smelling dead tissue, surrounded by a more or less extensive area of pneumonic consolidation. Older cavities have smooth fibrous walls and may be crossed by branches of the pulmonary artery and by thrombosed veins. Aspiration abscesses are most commonly situated in the apical or axillary broncho-pulmonary segments of the upper lobe, or in the dorsal segment of the lower lobe ; post pneumonic abscesses may occur anywhere, though the lower lobes are most commonly involved. Pleural effusion or empyema may develop. Gangrene of the lung differs pathologically from abscess only in that it is more extensive, and that the patient often dies before cavitation takes place. The lung is œdematous, necrotic, and diffluent, and may be black, brown, or greenish-grey in colour. A widespread pneumonia is present in the remaining viable tissue around the periphery of the gangrenous area.

Symptoms.—In aspiration abscess the symptoms are not obscured by a preceding pneumonia ; one or two days after the inhalation of infected material, cough, pleurisy, and pyrexia develop, and after an interval purulent sputum appears. The sputum may be tinged with blood, and after rather more than a week it becomes extremely offensive ; on examination it resembles that found in bronchiectasis, but contains shreds of lung tissue. The pyrexia is of the hectic type, cough becomes more and more distressing, and large quantities of sputum are brought up during the twenty-four hours. After profuse expectoration the patient is usually temporarily better. If bronchial drainage is adequate the symptoms may subside and the abscess heal ; more frequently it fails to do so and the clinical features of advanced bronchiectasis develop. Death occurs either from broncho-pneumonia, profuse hæmorrhage, cerebral abscess, or from gangrene of the lung. The last condition is manifested by high sustained pyrexia, rapid loss of flesh, and fœtid sputum which is fluid and of a greenish or dark brown colour.

Physical and Radiological Signs.—If the abscess is near the surface there will be signs of consolidation, or, more commonly, a pleural rub associated with limited movement, impaired note, a poor air entry, and râles. In some cases of chronic lung abscess the physical signs of a cavity may be present. Clubbing of the fingers soon develops, as may hypertrophic pulmonary osteo-arthropathy.

Before bronchial perforation has occurred X-ray films will usually show an ill-defined often nearly spherical dense opacity. When free bronchial communication exists, an air-containing cavity will be present, perhaps showing a fluid level, surrounded by more or less dense consolidation (*vide* Plate 26). A slough may be seen within the cavity. An opaque foreign body may be shown to be present. Bronchography may reveal secondary bronchiectasis, but the oil only rarely enters the abscess.

Diagnosis.—The history of pneumonia or of a recent upper respiratory operation, the toxæmia, offensive sputum, and the above signs are characteristic. The condition has to be distinguished from empyema, specially interlobar empyema, neoplasm, tuberculosis, and the more chronic forms of pneumonia.

Treatment.—Bronchoscopic examination is essential, as it may reveal a foreign body or a neoplasm as the primary cause of the abscess. About 40 per cent. of all cases of lung abscess heal, either spontaneously or as the result of purely medical treatment. This latter includes postural drainage, steam inhalations, and expectorants. Bacteriological examination of the sputum should be made, and penicillin therapy should be started forthwith and should be continued intensively if the infection proves susceptible. Spray inhalations may be combined with repeated intramuscular injections, 500,000 units daily being a suitable dosage. Mitras has devised catheters which permit transbronchial aspiration and subsequent lavage of lung abscesses with penicillin and has reported excellent results.

The majority of cases, however, react incompletely to these measures, and though each case must be judged individually, it is in general true that surgical intervention is more likely to be successful than continued medical therapy if the abscess is not healed two months after the onset.

Surgical therapy includes external drainage, lobectomy, pneumonectomy, and thoracoplasty, and may be combined with systemic and local penicillin administration.

NEW GROWTHS OF THE LUNG AND BRONCHI

Secondary Neoplasms.—Secondary growths are fairly common. Carcinomatous deposits may be secondary to cancer of the prostate, testis, breast, stomach, rectum, or any other organ, and are frequent with hypernephroma. Secondary sarcomata are usually either melanotic or metastases from a tumour in one of the bones.

Secondary growths are usually multiple and scattered in both lungs; those on the surface form umbilicated projections, while the deeper ones appear as pale rounded nodules. They cause an increasing dyspnœa, cachexia, and fever. Physical signs are often slight or absent until pleural involvement occurs. X-ray may show scattered "puff ball" shadows, while in carcinomatosis coarse "miliary" mottling affects all zones. The pleura is often ultimately involved. An effusion results, which is at first clear but later becomes blood-stained or purulent; in the fluid, clumps of malignant cells may be demonstrated.

Primary Neoplasms of the Lung.—These are very rare and include adenomatosis, endothelioma, and the more malignant primary sarcoma.

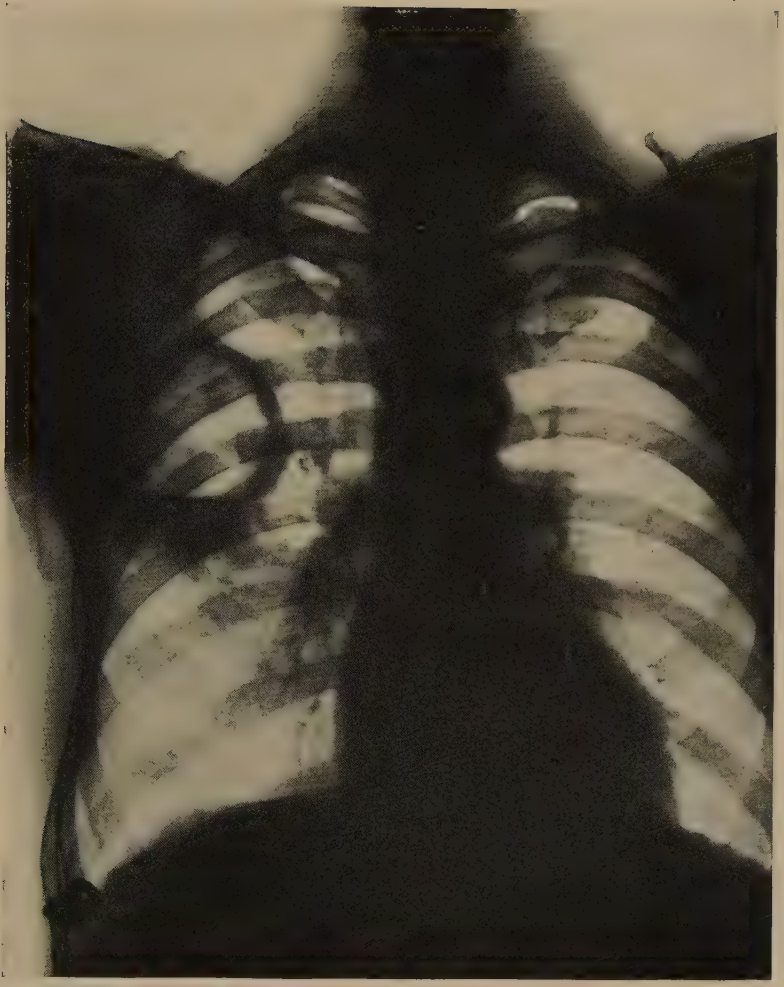

PLATE 26

Pulmonary abscess situated in the right upper lobe (axillary segment). The film shows a well-marked fluid level and dense surrounding pneumonia.

[*To face page* 474.

PLATE 27

Silicosis. Note the symmetrical distribution of the hard nodular shadows.

[*To face page* 475.

Bronchial Neoplasms.—The bronchial carcinoma is one of the more important forms of cancer, and is by far the commonest primary intrathoracic neoplasm. The incidence is highest in the fifth and sixth decades of life, and about five in every six occur in males.

The growth arises from the basal celled layer of the bronchial mucosa, usually near the hilum, and leads to bronchial obstruction, at first partial, later complete, with atelectasis and secondary pneumonia, bronchiectasis, or abscess. The growth may spread to local structures and frequently involves the pleura. In such cases a pleural effusion usually occurs which is commonly blood-stained, occasionally serous, and not infrequently secondarily infected. One in five of these growths originates in a small bronchus peripherally.

Metastasis occurs early in the mediastinal glands, and may spread thence to other lymph glands, while secondary deposits are commonly also found in the liver, brain, bones, kidneys, and other organs. The primary growth may be of the undifferentiated "oat-celled" type, or show attempts at the formation of alveoli, or it may undergo metaplasia giving rise to a squamous-celled carcinoma.

Primary innocent tumours of the bronchi are rare, and affect the sexes equally. They include adenoma, fibroma, lipoma, and chondroma. More frequently innocent tumours within the thorax are extra-pulmonary (*vide* p. 497). Innocent bronchial tumours cause cough, hæmoptysis, and ultimately bronchial obstruction with all its consequences.

Symptoms.—The early symptoms of bronchial carcinoma are cough, hæmoptysis, vague ill-health, and thoracic or upper abdominal discomfort. Later, dyspnœa, pain, lassitude, fever, weakness, and expectoration are added. The sputum is often blood-stained, the blood being dark and intimately mixed with mucopus, giving an appearance which has been likened to prune juice. Pain is generally not very severe, but it is remarkably persistent and differs from that of other pleuritic conditions in that it does not subside when effusion takes place. Dyspnœa may be extremely distressing, and may be accompanied by stridor, or a brassy cough. Wasting is not often severe. Secondary involvement of the mediastinal glands may lead to the mediastinal pressure syndrome described on page 497.

In many instances the predominating symptoms are due to septic absorption from pulmonary suppuration, from empyema, or the consequences of metastases. Death results in from six to eighteen months from cachexia, metastasis, right-sided heart failure, or sudden hæmorrhage.

Physical and Radiological Signs.—Effusion of fluid into the pleural cavity often masks the signs of the bronchial carcinoma. Aspiration may show the fluid to be blood-stained, and cytological examination may reveal tumour cells in the centrifugalised deposit, or in the particles of tissue remaining in the lumen of the needle. When there is no effusion, the signs are variable and include clubbing of the fingers, cyanosis, hypertrophic pulmonary osteo-arthropathy, and those of bronchial obstruction with its sequelæ (*vide* p. 450).

To postero-anterior and lateral X-ray examination localised emphysema, or atelectasis of part or the whole of a lung, with or without a hilar opacity, may be seen. On other occasions an opacity spreading out from the hilum is found, while a peripheral neoplasm commonly appears as a somewhat spherical uniform opacity. Secondaries in the mediastinal glands, septic complications in the lung, and pleural effusion frequently complicate these findings.

Bronchography may localise the site of the growth, as may tomography (*vide* Plate 24, p. 456).

Diagnosis.—In no disease is early diagnosis more desirable. Any of the early symptoms mentioned, if they occur in a patient past middle age, should arouse suspicion, and lead to investigation. At this stage there are no signs as a rule, and often an X-ray of the chest is normal. None the less, bronchoscopy and examination of the sputum by Dudgeon's method for carcinoma cells may identify a growth. The only bronchial neoplasm revealed with certainty by fluorography or X-ray examination before symptoms and signs arise is the peripheral type of innocent or malignant tumour. With the common type of bronchial carcinoma arising near the hilum, once bronchial obstruction has developed the well-marked and often characteristic symptoms, signs, and X-ray appearances set forth above arise. Bronchographic localisation with lipiodol is then seldom necessary, since the growth is accessible to bronchoscopy which will permit histological examination of a biopsy specimen. At the same time the distance of the growth from the carina, the fixity of the bronchus, and local distortion from glandular secondaries can be assessed, and will be of therapeutic and prognostic importance. In those cases in which, despite the above, doubt as to diagnosis still persists a thoracotomy may be justified.

Treatment.—In the great majority of cases treatment has at present to be palliative. It consists in the relief of pain with morphia when that becomes necessary, of oxygen therapy for dyspnœa, and the provision of comfort by good nursing. Irradiation, by radon or radium implanted locally into the growth, or by X-ray therapy, is as a rule only palliative, and may relieve pain or diminish sepsis by making the bronchus again patent. Occasionally, when the site of the growth permits and when diagnosis is sufficiently early, pneumonectomy may be curative.

THE PNEUMOKONIOSES

Pneumokoniosis is the term given to changes in the lungs resulting from the inhalation of certain dusts.

While a wide variety of organic dusts can cause bronchitis, and dusts such as those of arsenic and lead are dangerous on account of their poisonous properties, a limited group only, and in particular silica, causes the special forms of fibrosis of the lungs with which we are concerned.

The following varieties are described, depending on the nature of the dust causing the disease : anthracosis (coal), asbestosis (asbestos), lithosis (stone), siderosis (iron and other metallic dusts), and silicosis (silica).

Anthracosis is the most common, and is due to the inhalation of particles of carbon. It is found in all town-dwellers, and to a marked degree in coal miners. The carbon is present in the lymphatics, pulmonary lymph nodes, and in the mediastinal lymph glands. In advanced cases it is also found under the pleural surface of the lungs, and may even choke alveoli. Anthracosis, if uncomplicated by silicosis, produces little structural damage apart from choking the lymphatics, and it causes no symptoms. There is reason to believe that it may afford some protection against tuberculosis.

The inhalation of dust containing silica causes in time a characteristic nodular fibrosis of the lungs. The extent and speed of production of this

change have been shown to be directly proportional to the quantity of the dust inhaled and to its content of silica. It has also been shown that the pathogenic particles are always less than 10 μ in diameter and usually much smaller. Phagocytic cells remove the particles from the alveoli and pass in the lymph stream into the regional lymph nodes and glands draining the lungs. There a low-grade inflammation is set up by the contained silica, which eventually results in a fibrosis which chokes the lymphatic system. The fibrous replacement of the peripheral nodes at the bifurcations of the bronchioles gives rise to the characteristic "nodular" radiological appearance (*vide* Plate 27). Further inhalation in the presence of an inadequate lymph drainage results in more massive fibrosis within the lung parenchyma itself with a consequent massive widespread fibrosis characteristic of the advanced stages.

The change is slow and progressive, and may take from two to twenty or more years to be demonstrable. Clinically dyspnœa is the outstanding symptom. It at first limits and later abolishes any capacity for work, and with it is associated an unproductive cough, transient pleural pains, and bronchial colds. Cyanosis is present only in advanced stages of the disease. The physical signs are never commensurate with the symptoms of the disease, but in an advanced case the thoracic wall tends to be rigid, smoothly flattened in front, with raised shoulders, and movement is symmetrical but very limited. The percussion note may be resonant from associated emphysema, though patches of dullness from thickened pleura are not uncommon. The breath sounds are vesicular, distant, and characteristically dry. There is no fever, and except in extreme degrees of the disease no tachycardia, asthenia, expectoration, or hæmoptysis, all of which may quickly appear upon the supervention of tuberculosis, to which cases of silicosis are especially prone. Throughout the disease the sputum contains silica particles which may be demonstrated microscopically, using polarised light.

Siderosis, lithosis, and many examples of anthracosis are even slower in development. The pathology is similar, and it seems probable that they are examples of silicosis in which the choking of the lymphatic drainage of the lungs by a primary silicotic fibrosis is complicated by the concurrent retention of metallic, calcareous, and carbon particles respectively.

Asbestosis is the best known of several rare types of pneumokoniosis caused by silicates. The pathology is probably essentially similar to the above, but the fibrosis is always more diffuse. Radiologically nodulation is absent, and a reticular fibrosis, pleural thickening, diaphragmatic involvement, and a shaggy heart outline predominate. The clinical signs and symptoms are those of silicosis, save that the disease usually takes longer to develop. The sputum, however, on simple microscopic examination contains "asbestos bodies" which characteristically resemble brown translucent elongated dumb-bells; their presence is diagnostic of the condition.

All forms of pneumokoniosis tend to be steadily progressive, and the prognosis is unfavourable unless the individual is removed from the danger of further inhalation in the early stages of the disease. Complications include tuberculosis, chronic bronchitis, emphysema, bronchiectasis, and heart failure.

The most important therapeutic measures are preventive. They include devices which reduce the amount of dust inhaled, by the use of respirators and masks, efficient ventilation, and the free sprinkling of water to prevent

the formation of dust. Periodical medical and radiological examination of all who are employed in occupations with this hazard permits the exclusion of phthisis, and allows the diagnosis of pneumokoniosis to be made early in the disease. In established cases the treatment is that of chronic bronchitis and emphysema, while in advanced cases therapy is purely palliative.

ALLERGIC CONDITIONS OF THE RESPIRATORY SYSTEM

Some individuals are especially prone to allergic phenomena, *i.e.*, to sensitisation by foreign proteins, and suffer from anaphylactoid symptoms when exposed to the protein to which they have become sensitised. Manifestations in the respiratory tract are of two types—hay fever and spasmodic asthma. These two diseases are common in certain families, some members of which may be subject to one form and some to the other, while some unfortunate individuals are subject to both hay fever and asthma. The symptoms often commence in early childhood, but the onset may be delayed until the second decade or later ; after the fortieth year susceptibility to hay fever diminishes and the disease tends to die out. The incidence of both hay fever and asthma is highest in educated persons of nervous temperament and in town-dwellers.

HAY FEVER

Hay fever is a severe temporary catarrhal condition of the mucous membranes of the nose and throat and of the conjunctiva, which is due to sensitisation to the pollen of certain plants.

Ætiology.—Sensitisation of a susceptible individual takes place as a result of exposure to large quantities of wind-borne pollen, and the symptoms recur each year and coincide with the pollination of the particular plant causing the disease. In nearly all cases this pollen belongs to one of the common grasses, *e.g.*, timothy grass in Great Britain and ragweed in America. Timothy grass pollinates in May, June, and July, and it is in these months that the symptoms occur. In the United States the disease is also caused by tree-pollen in April and by the Compositæ (daisies, etc.) in the late summer.

Sensitive subjects develop symptoms of hay fever when the protein of the specific pollen is applied to the mucous membrane of the nose, throat, or conjunctiva, or when it is injected subcutaneously. Identification of this pollen is best carried out by skin tests in which the various pollens or their extracts are injected intradermally or are applied to superficial scratches on the skin of the forearm. A positive reaction is shown by an urticarial wheal surrounding the scratch. If more than one pollen provokes a positive reaction, the test should be repeated with increasing dilutions of the extracts, when the specific pollen will be found to give a positive test in dilutions often ten times as high as the others.

Symptoms.—The symptoms recur at the same season each year, usually from May to July. They do not persist throughout this period ; there are periods of remission and exacerbation corresponding with variations in the amount of pollen suspended in the air. The attacks commence with itching and burning sensations in the eyes and nose, followed by profuse lachrymation, running from the nose, and sneezing. There is usually some malaise, and

occasionally severe headache and depression. The affected mucous membranes become red and swollen, and some œdema of the eyelids is common.

Diagnosis.—The condition is distinguished from coryza by its regular recurrence in the early summer, and the diagnosis is confirmed by skin sensitisation tests with the grass pollens.

Treatment.—Treatment should be commenced twelve weeks before the date when symptoms are expected. The specific pollen having been identified, further skin tests are made to determine the greatest dilution which will provoke a local reaction. An extract which is just too dilute to provoke a reaction is then selected, and 2 minims of this solution are injected subcutaneously. A series of injections are given at five- or seven-day intervals, the dose being at first doubled on each occasion ; if symptoms of hay fever follow an injection, the next dose must be reduced and further increase made with caution. Pre-seasonal treatment is the most useful, but in some cases benefit is derived from a continuance of the injections throughout the period of pollination. This treatment is successful in diminishing the intensity of the symptoms in the great majority of cases, and completely prevents them in about 10 per cent. ; it must be repeated each year.

When the symptoms have become manifest they can only be abolished by removal of the patient from contact with the specific pollen by sending him to a mountain resort or on a sea voyage. He may obtain some relief by wearing dark glasses, by the subcutaneous injection of increasing doses of adrenaline, spraying the nose and conjunctivæ with a solution of adrenaline 1 in 5,000, or by taking $\frac{1}{2}$ gr. tablets of ephedrine hydrochloride twice a day. Benadryl or antistin tablets are also of value.

ASTHMA

Spasmodic asthma is characterised by recurrent attacks of dyspnœa in which the expiratory movements are laboured and ineffective. The dyspnœa is due to partial obstruction of the smaller bronchi by contraction of the plain muscle in their walls and by turgescence of their mucous lining. Exceptional cases occur in which the dyspnœa is inspiratory.

Ætiology.—The musculature of the bronchi is innervated by the vagus, and experimental stimulation of this nerve, either peripheral or central, causes contraction of the smaller tubes, with all the symptoms of an asthmatic attack. Expiration, being a comparatively feeble and passive act, is interfered with to a greater extent than inspiration ; consequently the lungs become over-distended with residual air, and dyspnœa with cyanosis results.

Asthma is regarded as an allergy comparable with urticaria or hay fever, and has in many instances been shown to be caused by sensitisation to specific foreign proteins. It is also significant that psychoneurosis, particularly anxiety neurosis, may complicate the disorder, and furthermore a family history of the disease or of a related allergic condition is very frequently encountered.

The allergen causing asthma is often one which is inhaled in the form of dust. The most provocative are dust-proteins, dandruffs from the coats of animals and poultry, pollen from certain plants, and powdered organic matter such as moulds, or feathers. The proteins of infecting organisms are responsible for a large proportion of the cases. In these the organisms are

often recoverable in pure growth from the sputum following an asthmatic attack; amongst those commonly found are the *Streptococcus viridans*, pneumococcus, Friedländer's bacillus, and *Micrococcus catarrhalis*. In a small group the attacks are due to ingested protein in the form of eggs, one of the cereals, or the flesh of a mammal, bird, or fish. Rarely an injection of serum, a bite or sting may initiate an attack.

The allergen sometimes is suggested by careful analysis of the history of the case; the symptoms may date from an attack of pneumonia or bronchitis; attacks may occur only when the patient stays in certain localities or houses where he comes in contact with one of the domestic animals, or when he partakes of a certain food. Confirmation should be sought in skin sensitivity tests as described above, using one of the proprietary protein-extract sets; or alternatively the suspected proteins are applied to the cutaneous incisions direct, and a drop of 10 per cent. sodium hydroxide solution is added in order to render them soluble. It is generally agreed that food proteins are seldom the cause of asthma which commences after childhood. Cases of asthma which clearly follow an acute respiratory infection should not be confused with those of asthmatic bronchitis, in which bronchial spasm occurs in subjects of chronic bronchitis and emphysema. Asthmatic bronchitis differs from spasmodic asthma in that the distress is as much inspiratory as expiratory, the attacks do not begin and end with the same abruptness, and the patient is not free from signs and symptoms of respiratory disease between the attacks.

Asthma is commonly more severe during menstruation; it is less severe, or absent, during pregnancy or a febrile illness.

In infants and some children asthma is accompanied by bronchiolitis and bronchitis; in other affected children eczema or prurigo are associated.

Symptoms.—At all ages the paroxysm occurs most commonly during the night; the patient is awakened by a feeling of suffocation, he sits up, and his breathing becomes more and more laboured; the expirations become longer and more wheezing, and in spite of bringing all the accessory muscles into play, fail to deflate the lungs before being interrupted by another short and spasmodic inspiration. The lungs become more and more distended and the thoracic movements more restricted; the face is pale and anxious and the finger-tips cyanosed, but the pulse-rate is little affected. At the height of the attack the patient is shaken by a paroxysmal cough; the sputum is at first scanty and viscid, then the secretion becomes more fluid and copious, the spasm relaxes, and the patient sinks back relieved but exhausted. Vomiting often terminates the attack in a child. Attacks last from a few minutes to several hours, and may recur the same night, or only after an interval of weeks or months. After many attacks of ordinary duration an attack may fail to terminate spontaneously, and continuing for several days and nights (status asthmaticus) may prevent sleep and the taking of food, and yield only to drastic treatment, or in rare instances may even result in death from cardio-respiratory failure.

In other cases persistent wheezing with dyspnœa intensified by emotion or exertion, and an ineffective cough, may largely replace acute attacks.

Physical and Radiological Signs.—During an attack the thorax is distended and the respiratory excursions are much diminished in spite of forcible muscular efforts; there are hyper-resonance and obliteration of cardiac dullness. The inspiratory murmur is short and feeble, while expiration is

greatly prolonged and accompanied by innumerable fine and medium rhonchi ; later râles predominate. Cyanosis, sweating, tachycardia, and a subnormal temperature are frequent.

The sputum is at first viscid and comes up in white lumps, the so-called " pearls of Lænnec." When unrolled these lumps are found to consist of mucous spirals, forming moulds of the smaller tubes. In addition to these casts, which are known as Curschmann's spirals, there may be eosinophil leucocytes and octahedral crystals (Charcot-Leyden crystals). Eosinophilia, varying from 5 to 30 per cent. of the total white cells, occurs, as does hypochlorhydria. These characteristics of the sputum, gastric juice, and blood count are inconstant.

The radiological findings during an attack are those of emphysema ; between attacks the appearance of the lungs may be normal.

Prognosis.—In children asthma sometimes clears up spontaneously, but, unlike hay fever, it does not show the same tendency to disappear after middle age. When spontaneous recovery takes place it is usually due to a change of the patient's environment. It is doubtful whether death has ever been caused by uncomplicated asthma ; but in old-standing cases chronic bronchitis and emphysema nearly always develop, and then status asthmaticus may be fatal. Such patients are also prone to broncho-pneumonia. Occasionally a lasting cure may be effected by suitable treatment. Complete recovery, however, is rare and limited to the relatively early case.

Diagnosis.—Any of the causes of obstruction of the larynx, trachea, large or small bronchi may simulate asthma. The family and personal history, the nocturnal paroxysmal attacks, skin reactions, eosinophilia, and response to adrenaline will usually characterise asthma.

Attacks of breathlessness with wheezing respirations occur in association with severe disease of the heart or kidneys. In " cardiac asthma " (*vide* p. 411) there are signs and symptoms of left ventricular failure, while " renal asthma" is accompanied by signs of nephritis with uræmia, such as renal retinitis, albuminuria, and a high blood urea. In both, cardiac hypertrophy and raised blood pressure are common.

Treatment.—*Prevention of Attacks.*—If the history, skin tests, and elimination diets have indicated a specific allergen much can be done to avoid or remove the irritant. Examples include, for instance, the substitution of rubber or kapok bedding for feather stuffed articles ; the vacuum cleaning of rooms ; and the use of cosmetics free from orris root.

Most asthmatics should accustom themselves to wide open windows, should shun crowded entertainments, and should be vaccinated against common catarrhal infections. Desensitisation is often necessary. If the patient, as is common, is found to be sensitive to more than one inhalent allergen a solution of the appropriate extracts is used ; or if one, such as pollen, is found to be specific for the case it should be employed alone. A course of subcutaneous injections slowly increasing in amount may be given twice weekly over several weeks, or, if necessary, may be concentrated into a few days if close medical supervision is provided, and adrenaline (3 minims of 1 in 1,000 solution) is injected at the same time to prevent an asthmatic reaction. Similarly, in cases due to infection an autogenous vaccine from the sputum should be used. The first dose should be small, amounting to 2 or 3 million organisms, and subsequent doses may be increased by 2 million organisms on each occasion.

Many asthmatics find that swallowing ½ to 1 gr. of ephedrine just before going to sleep prevents attacks of nocturnal asthma developing. The tablets should be swallowed whole and not dissolved in the mouth.

Encouragement from the medical attendant is always valuable; in selected cases psychotherapy may be of help. In asthma due to food proteins the only effective treatment is avoidance of the offending foodstuff.

Non-specific protein therapy in the form of intramuscular injections of peptone is occasionally beneficial, as may also be a similar injection of 10 c.c. of the patient's blood.

Constitutional Treatment.—Measures for the improvement of the patient's general condition are sometimes remarkably effective in diminishing the tendency to asthma; sources of sepsis should be dealt with, hypochlorhydria should be remedied, and a hygienic regime should be ordered. Heavy meals must not be taken in the evening, as they are likely, by producing gastric distension, to provoke attacks. Climate has an important influence on many asthmatics, and if a locality is found in which the patient is free from attacks, he should, if possible, make his home there. Operations on the nose and throat should be performed only for the elimination of gross sepsis. Women may become affected by asthma on reaching the menopause, and such cases appear sometimes to be cured by administration of thyroid extract. Sleeplessness should be relieved by bromides or luminal, and a codeine linctus may be used for nocturnal cough.

Many asthmatic subjects are more liable to attacks when lying down; they should therefore learn to sleep with the head and shoulders raised on four or five pillows.

Breathing exercises are very valuable. The correction of faulty posture and muscle relaxation are first taught. Then exercises are learnt and practised in order to co-ordinate and re-educate muscle action involved in the act of breathing, particularly in expiration.

Treatment of an Attack.—Adrenaline is incomparably the best drug both for the relief and abortion of an asthmatic attack. It is given hypodermically, and 1 or 2 minims of a 1 in 1,000 solution often give complete relief if administered as soon as the symptoms commence; if the attack is fully developed 3 or 4 minims should be injected and, without withdrawing the needle, a further minim given every thirty seconds until relief is obtained. It is therefore advisable to train the patient to give himself the injection. Cardophyllin may be used as an alternative to adrenaline. In some cases ephedrine gives similar relief, and it has the advantage that it can be taken by mouth, the dose being ½ gr. (⅛ to ¼ gr. for a child) of ephedrine hydrochloride. Benadryl, thiamin, and occasionally 10 gr. of aspirin may prevent or relieve an attack. Injections of morphia should not be used. They increase bronchial spasm, depress the respiratory centre and so augment anoxia, ultimately demoralise and not infrequently kill the patient.

For status asthmaticus, however, if frequent small doses of adrenaline should fail, injections of a solution containing ¼ gr. of morphine, $\frac{1}{100}$ gr. of atropine, adrenaline (1 in 1,000) to 10 minims, may be given every five minutes in 1 minim doses until the attack is relieved or the 10 minims have been injected.

For oral administration the most useful drugs, apart from ephedrine, are tincture of lobelia, grindelia, or stramonium in 15-minim doses, combined in a mixture with potassium iodide.

PLATE 28

Right-sided spontaneous pneumothorax. The right base is only partially collapsed. (From film by Dr T. H. Hills.)

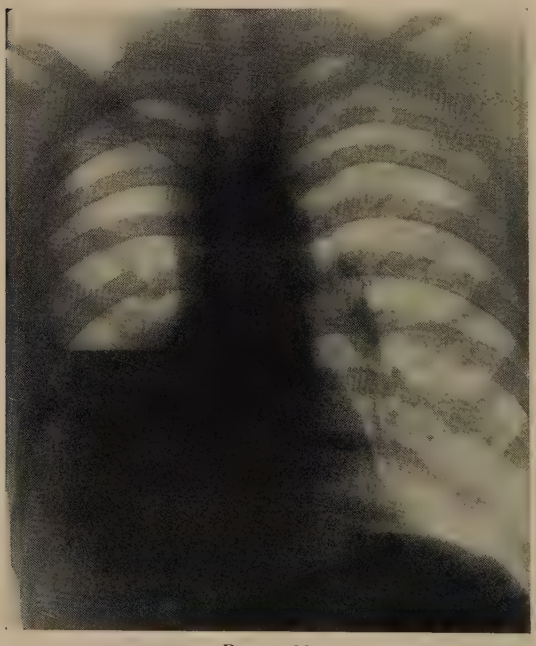

PLATE 29

Right-sided hydro-pneumothorax. The fluid level and the absence of lung markings in the upper part of the right chest should be noted. (From film by Dr T. H. Hills.)

[*To face page* 483.

DISEASES OF THE PLEURA

Spontaneous Pneumothorax

In some instances the entry of air into the pleural cavity, in the absence of external trauma, is due to rupture of a tuberculous cavity or focus into the pleura. By this means a fistulous opening is formed, connecting the pleural cavity with one of the smaller bronchi. With each inspiratory movement air is drawn into the pleural cavity and the lung recedes from the chest wall. If the opening is a valvular one, a considerable positive pressure will be attained, and the heart and mediastinum will be displaced to such an extent that death may quickly result. Tension pneumothorax is rare, since with collapse of the lung the opening usually becomes sealed before the intrapleural pressure rises to a dangerous height.

The onset may be insidious and the condition may be discovered accidentally, but usually it is marked by a sudden stabbing pain in the side, dyspnœa, cough, and in tuberculous cases pyrexia, and effusion of fluid into the pleural sac. Artificial pneumothorax is quite often complicated by the spontaneous variety.

The majority of cases of spontaneous pneumothorax, however, are due to causes other than tuberculosis. The commonest is probably the rupture of an emphysematous bulla, an accident which is apt to recur in the same patient, often after an interval of years. In such cases a fluid reaction is rare unless as very occasionally happens the rent in the lung involves a blood-vessel of considerable size, and a hæmo-pneumothorax results.

Physical Signs.—The signs vary in proportion to the amount of air which gains entrance to the pleural cavity. A small collection, limited by pre-existing pleural adhesions, may defy detection except by stereoscopic skiagraphy. Larger amounts, even if sufficient to cause generalised collapse of the lung, may be overlooked by good clinicians ; for when the underlying lung is nowhere atelectatic, there may be no abnormal signs whatever, except diminution of the breath-sounds in the lower part of the affected hemithorax. With a considerable spontaneous pneumothorax, however, we find all the classic signs which make diagnosis easy. On inspection there is impairment of movement and the heart and trachea are displaced towards the unaffected side. The sternomastoid muscle is prominent on the side of the lesion. On percussion the note is hyper-resonant ; on auscultation the breath-sounds are absent or distant and amphoric in type. An amphoric cough and tinkling râles are heard if a bronchopleural fistula is present. If an assistant presses a coin flat on the chest wall and strikes it with a second coin, the examiner, listening with his stethoscope over another part of the pneumothorax, may hear a clear, ringing note, the " bell sound " or " coin sound." Voice conduction is usually not materially altered.

X-ray shows peripherally an absence of lung markings and the lung collapsed toward the hilum on the affected side. On screening, the mediastinal displacement is seen to be most marked on inspiration (*vide* Plate 28).

Treatment.—The patient is confined to bed, and if he is suffering from shock should be given morphia and kept warm. If the pleural cavity is overdistended and the patient distressed, air must be withdrawn, and temporarily a continuous water-sealed drainage may be required for the

" tension " type (*vide* p. 490). Cough should be checked by a codeine linctus. Rest in bed should continue until to radiological examination the lung is shown to have re-expanded completely. If two or more recurrences take place it may well be desirable to induce adhesion of the pleural surfaces by blowing iodised talc on to the visceral pleura at thoracoscopy. Despite the absence of X-ray or other evidence of tuberculosis, it is a wise precaution to re-examine the patient at three-monthly intervals during the next year.

Effusions complicating Spontaneous Pneumothorax

Spontaneous pneumothorax caused by the rupture of an emphysematous bulla is as a rule not complicated by the development of an effusion. Occasionally, however, radiological examination will demonstrate a collection of fluid in the costophrenic angle, too small otherwise to be detected, which represents the reaction of the pleura to a few drops of blood shed at the time the lung was torn. An effusion often develops when spontaneous (or artificial) pneumothorax is associated with active pulmonary tuberculosis. The condition which results is called *Hydropneumothorax*, and it is due to tuberculosis of the pleura. The fluid is an exudate and has the chemical, cytological, and bacteriological characteristics of that found in pleurisy with effusion (*vide* p. 487). The constitutional symptoms caused by the pleural infection also resemble those of that disease. They vary in severity and include fever, pallor, sweating, anorexia, loss of weight and strength, and sometimes diarrhœa and dyspepsia. A normochromic anæmia develops in the more severe cases. In addition, since the fluid by its bulk enhances the mechanical disability caused by the pneumothorax until the mediastinum becomes anchored by adhesions, the sensation of pain and tightness in the chest, and dyspnœa, are augmented as the fluid accumulates. Cough and cardiac palpitation are also increased, while the patient may notice a splash on movement.

The physical and radiological signs are characteristic. As well as the signs of pneumothorax there are found below dullness to percussion, the upper limit of which remains horizontal whatever the posture of the patient, and absence of breath sounds, vocal fremitus, and resonance over the fluid; and also, if appreciable amounts of fluid are present, an audible splash on shaking the patient. If the bronchopleural fistula is still open, bronchial breathing, an amphoric cough, tinkling râles and a coin sound will be heard over the pneumothorax. A radiogram shows the pneumothorax, the collapsed lung, the mediastinal displacement, and the opaque fluid with its horizontal upper level. Fluoroscopy will also demonstrate in an early case that the mediastinum moves laterally to and fro on respiration.

If the underlying lung becomes atelectatic the extent of the mediastinal displacement will be considerably lessened, or with a small hydropneumothorax may be abolished, or even on occasion the heart may be displaced toward the affected side.

All these signs change as adhesions develop and fluid and air are absorbed. The affected side of the chest tends to move less and become flat, the heart and trachea move back and may at length become displaced into the hydropneumothorax, while pleural thickening may be so marked that the percussion note over the affected side may be dull and air entry permanently diminished.

A specimen of fluid should always be obtained for cytological and bacteriological examination. Commonly therapy is that of pleurisy with effusion, and with rest in bed the air and fluid will slowly be absorbed. Thereafter prolonged convalescence or sanatorium treatment is desirable.

If the bulk of the pleural contents embarrasses respiration, sufficient fluid should be removed to give relief. The procedure may need repetition. As a rule the fluid contains only a few tubercle bacilli or remains sterile, and is slowly reabsorbed.

Pyopneumothorax.—In a minority of cases of hydropneumothorax the number of tubercle bacilli in the fluid rapidly increases and pyogenic organisms not infrequently also appear. Usually in these cases the tearing of adhesions containing lung tissue or the rupture of a tension cavity into the pleura result in the formation of a large broncho-pleural fistula. The patient soon becomes seriously ill, gross toxæmia being added to the symptoms described above and to those of active tuberculosis from which he is suffering. The prognosis is grave whatever the treatment, and a majority of these cases die within a few months. Repeated aspiration, combined, if the pyogenic infection is penicillin sensitive, with local and systemic penicillin administration is occasionally successful in overcoming the infection. Sinus formation tends to take place along the needle tracks and local promin applications to these may be of assistance in promoting their healing. A temporary closed drainage with suction, the site of the drainage being placed well clear of the area of incision usually chosen for thoracoplasty, is sometimes desirable, and if this method is used it should be used early. As a rule, however, only a thoracoplasty can close the cavity in the pleura and the bronchopleural fistula, and provide adequate surgical collapse therapy for the underlying pulmonary tuberculosis. Since the operation may have to be done upon a patient who is usually seriously ill the results are relatively disappointing. Non-tuberculous pyopneumothorax complicating, for example, lung abscess, suppurative pneumonia, or following infection in a hæmopneumothorax, should be treated as an empyema and will require at first closed and later probably open drainage.

Hæmothorax and Hæmopneumothorax

Hæmothorax may arise spontaneously, with or without simultaneous entry of air to the pleura, as a result of a tear in the surface of the lung. The ætiology of these cases is probably essentially similar to that of spontaneous pneumothorax. Hæmothorax also occurs in various blood diseases such as purpura and leukæmia, from a leaking aneurysm, in association with malignant neoplasms, both primary and secondary, and blood commonly enters the pleural cavity from the chest wall or lung following penetrating or non-penetrating injuries. Chest-wall hæmorrhage, often associated with fractured ribs, may need local surgical intervention.

Even if hæmorrhage stops, the bulk of the effusion is always augmented during the next day or so by exudate from the pleura. A large hæmothorax produces symptoms of loss of blood together with dyspnœa and pain in the chest, and the physical and radiological signs are usually those of pleural effusion. The lesion gives rise to considerable pyrexia, so that the advent of infection can only be judged by bacteriological examination of a sample removed at thoracentesis. If the fluid is purple and has an offensive smell, infection may be presumed. In these cases preliminary closed (under water)

drainage by intercostal catheter is usually deemed advisable, and therapy subsequently is that of an empyema. In the absence of infection, uncomplicated traumatic hæmothoraces are best treated from the onset by repeated aspiration. The pleura should be kept as dry as possible, though the volume of blood removed at a thoracentesis should at first be small. In rare cases of clotted hæmothorax, thoracotomy with removal of the contents may be necessary. Since associated pulmonary atelectasis is common the diaphragm beneath the hæmothorax may be unexpectedly high; this should be remembered when aspirating or draining the lesion.

Hæmopneumothorax is common when the lung or chest wall is lacerated and should be treated on the above lines. It may, however, also develop as a result of gas gangrene though the visceral pleura is intact. Pressure symptoms are then added to the toxæmic effects of the infection. In cases due to blood diseases or to neoplasms the hæmothorax is symptomatic and its local management is but one part of the general treatment required by the patient.

Prophylactic chemotherapy and immunotherapy are especially essential in all cases of traumatic hæmothorax, and this treatment may later be repeated if infection develops. Blood transfusion is often necessary, while oxygen therapy is of less importance. As soon as danger of further hæmorrhage from the original lesion has passed, breathing exercises should be started and continued, so that the fullest possible respiratory function may be restored.

Chylothorax

This term is applied to effusions of milky fluid into the pleural cavity. In a true chylothorax the fluid contains fat droplets and originates from the thoracic duct or its tributaries as a result of rupture or obstruction. The cases most commonly encountered are either due to trauma, such as a penetrating wound, or to malignant neoplastic involvement of the duct.

An effusion, which to the naked eye looks milky, called a chyliform effusion, occurs in long-standing tuberculous empyemas and very rarely in chronic pyogenic empyemas. Microscopic examination of the fluid shows it to contain degenerate pus cells and endothelial cells undergoing fatty degeneration. Cholesterol crystals may also be present in the fluid. Treatment is that of chronic empyema.

Hydrothorax

This is a non-inflammatory transudate of clear fluid into the pleural cavity. It usually occurs in conditions causing dropsy such as congestive heart failure, nephritis, or starvation œdema. In congestive heart failure the effusion is frequently unilateral (usually on the right side). Obstruction of the great veins by conditions such as lymphadenoma or chronic mediastinopericarditis may also produce a hydrothorax. Effusions, which are frequently intermediate in composition between a transudate and an exudate, may be found in the rare conditions of polyserositis.

Pleurisy

Pleurisy is an inflammation of the pleura, which may become covered with a fibrinous membrane—" dry pleurisy "—or separated by a liquid exudate. If the fluid is clear the condition is known as " pleurisy with effusion " and,

if purulent, as "empyema." These conditions are to be distinguished from non-inflammatory transudates such as hydrothorax, hæmothorax, and chylothorax, which are fluid collections resulting from lesions other than pleurisy.

Ætiology.—When the evidence of inflammation is confined to the pleura the condition is termed "primary pleurisy." This not infrequently follows trauma or exposure to cold but in many instances is due to tuberculosis.

Secondary pleurisy is usually due to extension of disease from the lungs and is a feature of pneumonia, tuberculosis, bronchiectasis, bronchitis, pulmonary abscess, infarct, and neoplasm; less commonly it is due to extension of inflammation from neighbouring structures, as in pericarditis, mediastinitis, subphrenic abscess, bronchial lymphadenitis, and Hodgkin's disease; it may be due to metastatic infection from tonsillitis or septicæmia, or be part of a general disease such as acute rheumatism, and it is commonly associated with certain chronic diseases such as nephritis.

Bacteriology.—Exudates accompanying acute pulmonary disease usually yield a growth of pneumococci or streptococci, but staphylococci, Friedländer's bacillus, and influenza bacilli are sometimes found. The importance of tuberculosis as a factor in the production of pleurisy has already been stressed (*vide* pp. 89 and 100).

Morbid Anatomy.—The pleura is at first congested and loses its naturally smooth, shiny appearance; next, an exudate of fibrin forms, varying in amount from a delicate film to a pasty coating $\frac{1}{2}$ in. in thickness. If absorption and organisation takes place at this stage, permanent adhesions will be formed, but in many cases the dry fibrinous exudate is followed by a serous effusion. The fluid is at first clear, but may later become turbid from the presence of leucocytes, or even purulent. A blood-stained effusion is usually associated with malignant growth, tuberculous disease, or pulmonary infarction.

The fluid in inflammatory exudates has a high specific gravity, 1,015 or over; it is rich in protein and contains a large number of cells. These are mainly polymorphonuclear leucocytes, except in tuberculous effusions, which show a predominance of this type of cell only in the early stage, being replaced later by lymphocytes. Bacteria are usually found in films or cultures, except in the tuberculous cases, and in these the nature of the infection can usually be demonstrated by culture or injection of the fluid into a guinea-pig.

The fluid of a non-inflammatory transudate is sterile; it is of a lower specific gravity, 1005 to 1015; contains less protein, 3 per cent. or under; and there are few cells, which are chiefly lymphocytes and endothelial cells.

A small effusion, persisting for only a few weeks, leads to little structural change in the chest apart from adhesion of the pleural surfaces after they have resumed contact. A large effusion, on the other hand, if allowed to remain over a long period, causes collapse of the underlying portions of the lung and so much thickening of its pleural covering that re-expansion may never take place. Fibroid changes then occur in the lung, and the chest wall falls in on the shrunken viscus.

Polyserositis, or Pick's disease, is a rare condition in which sero-fibrinous effusions occur in the pleura, pericardium, and peritoneum (*vide* p. 391).

Dry Pleurisy and Pleurisy with Effusion.—The symptoms, signs, and treatment of these conditions are outlined in the section on tuberculous pleurisy; they are not materially different when caused by other infections,

but are more apt to be overshadowed by disease in the lungs or other organs.

Pleurisy, especially pleurisy with effusion, is almost always tuberculous when it occurs in young subjects. After middle age it is frequently due to bronchial or secondary growths, or it may be due to pulmonary embolism.

Dry Pleurisy.—The chief symptom of dry pleurisy is pain, the character of which depends on the site of the inflamed area. Apical pleurisy causes no more discomfort than a dull ache, whereas inflammation of the more mobile parts near the lower margin of the lungs, or on their diaphragmatic surfaces, is characterised by sharp, stabbing pain which may amount to agony. This pain is greatly accentuated by coughing or the taking of a deep breath.

The characteristic physical sign is a friction rub, which is usually audible and sometimes perceptible as a tactile vibration on palpating the chest. Diaphragmatic pleurisy is not accompanied by this sign, but causes pain referred to the neck or abdomen, and by its simulation of acute abdominal conditions sometimes leads to an unnecessary laparotomy. Friction sounds in the upper part of the chest are sometimes caused by movements of the scapulæ, and should be excluded by altering the position of the patient's shoulder.

The pain of thoracic pleurisy is relieved by immobilising the affected side of the chest by strapping, and in diaphragmatic pleurisy a similar result is obtained by the application of a tight binder round the abdomen. Antiphlogistine, or other poultices, an electrically heated pad, or even artificial pneumothorax may be used.

Pleural Effusion.—The important signs of effusion are: diminished movement of the affected side of the chest; displacement of the heart towards the sound side; a flat percussion note over the lower part of the chest which reaches its highest point in the axilla; absence of voice sounds and of tactile vocal fremitus over the dull area. It should be noted that if the underlying lung is consolidated or atelectatic, bronchial breath sounds and ægophony will be heard through the overlying fluid.

With large effusions mediastinal displacement may give rise to dullness at the base of the sound lung near the spine.

X-ray examination shows an opacity obliterating the costophrenic angle. With large effusions the heart is displaced and the opacity apparently extends highest on the mediastinal and costal surfaces of the thorax, so that the upper edge of the effusion seems concave.

Fluid may be loculated by adhesions in any part of the pleural cavity, perhaps the commonest site being between the lobes. When loculated collections lie adjacent to the chest wall, localised dullness to percussion with absent breath sounds may be detected. Anteroposterior and lateral radiography will define the site of interlobar or other localised collections of fluid and will also, as a rule, show the presence of the adhesions which have caused the loculation, and thereby will assist in diagnosis.

Treatment.—The treatment of tuberculous pleural effusion is discussed on page 102. In other cases therapy is for the most part that of the underlying disorder. Thoracentesis, which confirms the diagnosis, is needed for the full investigation of the nature of the disease, and a small quantity of the fluid should in general always be removed for this purpose, so that, for example, the cytology and bacteriology of the effusion may be established. As a rule the aspiration of large quantities of fluid is unnecessary. Exceptions occur

when the effusion is so large that it causes respiratory and circulatory distress by its bulk, and when the effusion fails naturally to resolve. In the former instance sufficient fluid should be removed to afford relief of symptoms, and after a day or so the aspiration may, if necessary, be repeated. The total volume removed at one aspiration should not exceed 1 pint, since with larger quantities the risk of causing left ventricular failure with pulmonary œdema is significant. Radiological examination of the underlying lung is facilitated by thoracentesis, with or without air replacement. In non-tuberculous effusions air replacement is otherwise rarely justified.

Failure of an effusion to absorb, after say six weeks or more, is an indication for aspiration. The intravenous administration of calcium gluconate sometimes promotes more rapid reabsorption, while breathing exercises are in some cases justified and assist in the re-expansion of the underlying lung.

Convalescence of a restful nature is essential and should rarely be less than three months in duration.

CHEST WOUNDS

When a chest injury is sustained, shock, hæmorrhage, and later infection may any or all develop and imperil the patient's life. Since these sequelæ are common to all wounds their clinical features and therapy will not be elaborated here except in so far as they are modified by the special localisation of the lesion. It must be emphasised, however, that the early recognition, assessment, and treatment of these conditions are vital. In particular, the commensurate use of resuscitative measures such as the transfusion of blood, serum, or plasma, and oxygen administration, together with the employment of chemotherapy with anti-tetanus and anti-gas-gangrene sera as prophylactic measures against infection, are all procedures of the first importance.

Chest wounds have special characteristics because the thorax contains and is specially adapted to contain the lungs, the heart, and the great vessels. More or less severe impairment of respiratory and circulatory function may consequently follow this type of injury. Comprehensive yet simply applied tests of these functions have not yet been devised, therefore the assessment of a patient's condition in these respects, upon which appropriate therapy must be based, is largely dependent upon the ability of the clinician to evaluate the aggregate significance of the symptoms displayed, together with the extent of the anatomical damage which physical signs, radiological appearances, and other tests may show.

Injuries of the Thoracic Parietes.—The impact of missiles, and crush injuries, may result in isolated or multiple fractures of the ribs and sternum. Pain, cough, and dyspnœa commonly result, and the last in cases with extensive fractures may be fatal. It is dependent upon paradoxical respiration; for, as the intrathoracic pressure falls with inspiration, the now mobile chest wall moves inwards freely, and the alveolar air passes from the underlying into the opposite lung, while, on expiration the reverse process occurs, air passing back from the sound to the injured side. This paradoxical movement may be seen and felt, and is obvious at radioscopy, which will also reveal the coexistence of mediastinal oscillation. The author has found that severe cases of this type of dyspnœa are best treated by the use of a respirator such as the Nuffield modification of the Both machine now available in British hospitals.

Pain should be controlled by free injection of percaine around the site of the fractures, and the patient should remain in the apparatus until, with trial, the chest wall is shown to have recovered its stability. In less severe cases strapping and oxygen administration may suffice.

Hernia of the Lung.—A late consequence of fractures of the upper sternum or of the upper costal cartilages is hernia of the lung. The condition is painful, and the swelling is apparent on coughing or straining. A plastic operation is usually necessary.

Diaphragmatic Hernia.—Crush injuries and penetrating wounds may produce laceration of the diaphragm, which permits herniation of the abdominal viscera into the thorax. The great size of the liver usually limits hernia development on the right side, though if stomach or intestine is extruded through a diaphragmatic rent here, obstruction of the bowel is even more likely to develop than is the case on the left side. Symptoms and signs depend largely upon the size and contents of the hernia. The condition may only be discovered by chance at radiological examination or thoracotomy; with a large hernia, however, the symptoms and many of the signs of a large collection of air or fluid, or both, in the pleural cavity may appear. Mediastinal displacement may be gross, and commonly the symptoms and signs are much worse in the supine posture. Borborygmi and a splash may be audible. Radiologically it may seem probable that abdominal viscera are within the thorax, for colonic haustrations or the partly filled stomach may be identified. The probability will be increased if the upper border of the lesion is convex, and the suprajacent lung displaced towards the apex. In pneumothorax the lung collapses towards its root. A barium meal will confirm the diagnosis. Therapy is surgical, and repair of the laceration should be undertaken before vomiting and other evidence of intestinal obstruction have developed. It is usually desirable to empty the stomach completely by means of a Ryle's tube immediately before operation, and resuscitation may be a matter of urgency.

Surgical Emphysema.—Surgical emphysema of the mediastinum and chest wall may occur in association with pneumothorax, masks other signs, and only occasionally causes pain and distress. Crepitation on palpation, hyper-resonance, and crackling sounds on auscultation are diagnostic. Cough should be abolished with morphia, and reabsorption may be accelerated by continuous oxygen administration. Tudor Edwards has suggested the insertion of a curved needle behind the manubrium for the relief of dyspnœa in severe cases of mediastinal emphysema.

Pleural Lesions

Sucking Pneumothorax.—The diagnosis of this condition is obvious, for the lesion can be seen and heard. Paradoxical respiration occurs, and the abnormal lung movements can sometimes be seen through the wound in the chest wall. Immediate closure by packing and surgical means is essential, after which radiological and other investigations can be undertaken as the condition of the patient improves.

Tension Pneumothorax.—This lesion is not common but may arise from penetrating or non-penetrating wounds. The clinical and radiological evidence of its presence has been discussed (*vide* p. 483). A pneumothorax needle should be inserted, with aseptic precautions, through the chest wall 3 in. from the midline in the second interspace, and sufficient air withdrawn by a pneumo-

thorax apparatus to give symptomatic relief. If after coughing a rise in the recorded pressure then takes place, the needle should be connected by means of a long tube passing beneath the surface of water in a Winchester bottle, so that continuous drainage is insured until the valvular opening in the lung closes. In an emergency any wide-bore needle will suffice to reduce the pressure temporarily. If possible a rubber finger-stall with a small opening at its tip should then be tied securely over the butt, so that transport to hospital may safely take place. Coughing should be temporarily abolished with morphia.

Traumatic Pneumothorax.—Like spontaneous pneumothorax, this lesion frequently requires no special therapy save rest in bed, while the patient is under clinical and radiological observation. Complications such as tension pneumothorax, hæmorrhage, or infection can thus quickly be identified and treated, as may associated lesions.

Hæmothorax and Hæmopneumothorax (*vide* p. 485).

Pulmonary Injuries

Blast Lesions.—It seems probable that the impact upon the body of an explosion wave, whether conducted through air or water, is the causal factor. The lesions tend to occur at tissue-air interfaces, and are thus common in the lungs and intestines. In the lungs multiple small hæmorrhages, usually more extensively present on the right side, occur, some interstitial, some alveolar, associated with emphysema. As a result of both these lesions the pulmonary capillary bed is reduced in proportion to the severity of the lesion. Dyspnœa, cyanosis, cough, and pyrexia occur, as may hæmoptysis. Occasionally bronchial obstruction from clotted blood adds the complication of pulmonary atelectasis. The physical signs are usually insignificant, but may include an emphysematous appearance of the chest and scattered râles. Radiologically multiple opacities, indistinguishable from broncho-pneumonia, are seen, and occasionally serial examination during the first three days will disclose an increase in the lesions. The lesions absorb relatively rapidly, and the chest may be radiologically normal in less than a week. Oxygen therapy is of outstanding value, while general anæsthesia and transfusions of any kind should, if possible, be avoided until after recovery has occurred. Every patient exposed to the hazard of blast, therefore, needs early and repeated radiological examination.

Pulmonary Hæmatoma.—An isolated hæmatoma of the lung may follow a sufficiently severe blow on the chest wall, and bruising of the lung tissue in addition to laceration is commonly produced when high-velocity missiles penetrate the chest. A large hæmatoma has clinical consequences similar to those of an infarct of comparable size. Thus, pyrexia, cough, hæmoptysis, pleuritic pain, dyspnœa, and sometimes jaundice may result. The physical signs include superficial bruising, diminished movement and air entry, and an impaired percussion note. Only occasionally do the signs resemble those of consolidation. Radiologically an irregularly spherical opacity is often seen, and not uncommonly the edge of the lesion may be clearly defined. The size of the opacity may vary from a just perceptible shadow to one which involves a whole lung.

A majority of hæmatomata slowly resolve, and during this time the patient should rest in bed and receive symptomatic treatment. Breathing exercises

and oxygen therapy are of value, while occasionally secondary infection of the lesion will make drainage or other surgical measures necessary.

Pulmonary Atelectasis.—Lobar and multilobular atelectasis of lung occur commonly in association with a variety of chest wounds, and arise as a result of bronchial or bronchiolar obstruction by, for example, blood, sputum, rupture, or kinking. The signs, symptoms, radiological appearances, treatment, and sequelæ differ in no way from those described on page 460, save that rupture of a major bronchus will necessitate early removal of the involved area of lung.

Pulmonary Fat Embolism.—Bony fractures, and wounds involving fatty tissues, may be followed by fat embolism. The onset of symptoms generally occurs some seventy-two hours after the injury. The symptoms include apprehension, increasing dyspnœa, pleuritic pain, tachycardia, cyanosis, pyrexia, and cough productive of sputum which may be frothy or blood-stained, and which contains extracellular fat. Physical signs commonly consist of diminished air entry and râles at the bases of the lungs, though occasionally areas of consolidation may be detected. Not infrequently the clinical picture is complicated by the consequences of multiple fat emboli in the brain and spinal cord, while petechiæ in the skin are also often present. Radiological signs in the chest are usually those of multiple areas of consolidation, predominantly basal in site, while the general haziness of pulmonary œdema obscuring the lower lung fields is also sometimes seen. Major therapeutic measures include the prophylactic avoidance of all unnecessary movement of fractured bones, and in established cases oxygen therapy, venesection, and the general measures for the treatment of pneumonia.

Intrathoracic Foreign Bodies.—Radiology, and the use of anteroposterior and lateral films, will as a rule identify and localise a radio-opaque foreign body with accuracy. Anatomical localisation, *e.g.*, within a certain lobe of the lung, is usually all that is essential unless the lung is adherent to the chest wall, when depth measurements may also be necessary. Radio-translucent foreign bodies may be found at thoracotomy when surgical toilet of the track of the wound is carried out. If the condition of the patient permits it is in general wise to remove a foreign body at the earliest possible moment, *i.e.*, within six hours of the injury, for risk of infection and secondary hæmorrhage is thereby decreased. In practice this is not often possible and under these circumstances the intervening period is occupied in treating associated lesions, such as shock, hæmothorax, or wounds of the chest wall, in combating infection with chemotherapy and other measures, and in resuscitating and improving the general condition of the patient. The decision if and when to operate is determined by a multitude of factors, which apart from the condition of the patient include the size, site, and number of foreign bodies concerned. As a rule a thoracotomy is most urgent when there is evidence of continued intrathoracic hæmorrhage, when a large foreign body is retained, in cases of abdomino-thoracic wounds, and in those cases for which temporary closure of a sucking pneumothorax has already been undertaken. The operation is rarely if ever necessary in cases of clean stab or perforating wounds, and foreign bodies smaller in size than the little finger-nail may usually be left alone with safety. Until shock, hæmorrhage, or blast lesions of the lung have been adequately relieved operative intervention should be postponed, while similarly priority in treatment is usually required for hæmothorax. Surgical textbooks should be consulted for further details.

Cardiovascular Wounds

Pericardium.—Quite small quantities of blood in the pericardium give rise to pericarditis ; a large hæmopericardium, if the wound provides inadequate drainage, may accumulate rapidly and progressively diminish the ability of the heart to fill in diastole, and therefore cause an increasing distension of systemic veins and a fall in the cardiac output. Clinical evidence of the latter will be found in increased dyspnœa, tachycardia, and a fall in the arterial blood pressure. Local physical and radiological signs of fluid, or fluid and air in the pericardium, may be present. Perhaps a majority of these cases are best treated conservatively, particularly if pericardial drainage is adequate to prevent the development of a large hæmopericardium. Control of the latter should be attempted by aspiration. When possible a pneumothorax induction needle should be used and sufficient blood aspirated to give symptomatic relief. The pressure within the pericardium should then be recorded and the cannula left in position, so that if in the next few hours the pressure again rises aspiration may be repeated. If the lesion is not controlled in this way surgical drainage should be undertaken, at which operation it may be possible not only to repair the cardiac wounds but also to remove adjacent or impacted foreign bodies.

The pericardium may become infected directly, or by spread from nearby infected lesions. A pyogenic pericarditis results, and will usually require surgical drainage and chemotherapy. The presence of other lesions, such as pulmonary hæmatoma, or hæmopneumothorax, by masking physical and radiological signs frequently makes diagnosis difficult.

Retained Foreign Bodies.—A few cases survive and reach hospital with foreign bodies in the heart muscle or within the organ. Accurate localisation of the foreign body is often possible radiologically, and after adequate resuscitation, if the foreign body be large or sharply pointed, surgical removal with drainage of the pericardium should be attempted. When the foreign body is within the left ventricle or auricle it may be preferable to await its ejection and then remove it from a peripheral artery.

A foreign body adjacent to the heart may cause delirium cordis and gross circulatory collapse without inflicting anatomical damage to the heart. Such a complication constitutes an added reason for the early removal of the foreign body. Circulatory failure also accompanies many cases in which marked mediastinal oscillation occurs (*e.g.*, in massive collapse or pneumothorax).

Cardiac Contusion.—Occasionally the heart is crushed between the sternum and vertebral bodies, and in young subjects this may occur without fracture of the ribs or sternum. In a severe case the clinical course is that of coronary thrombosis, and since almost invariably the posterior surface of the heart is most damaged, an electrocardiogram will show changes associated with thrombosis of the right coronary artery. Oxygen therapy, venesection, and the treatment of cardiac infarction is required.

Wounds of the Great Vessels.—Rarely early operation may be successful in treating wounds of the great vessels. In other surviving cases aneurysm formation, including arteriovenous aneurysm, may result.

The early removal of foreign bodies adjacent to great vessels may prevent such a consequence, but once aneurysm formation has occurred therapy is largely palliative. In some cases of arteriovenous aneurysm, and occasionally

in the more peripheral intrathoracic cases of simple aneurysm, surgical therapy may be curative, and should be undertaken at a relatively early stage.

W. D. W. Brooks.

EMPYEMA

Ætiology.—Empyema is usually secondary to pulmonary disease, particularly lobar pneumonia, and less often broncho-pneumonia, abscess, or tuberculosis. Other causes are intrathoracic neoplasm, subphrenic abscess, liver abscess, leakage from a cancerous œsophagus, and penetrating wounds of the chest. The infecting organism is in most cases either a streptococcus or a pneumococcus, but the influenza bacillus, staphylococcus, and actinomyces are sometimes found. In tuberculous empyema the fluid is often sterile.

Morbid Anatomy and Pathology.—The wide ignorance of what constitutes an empyema and the looseness of thought and definition that result are the chief cause of many differences of opinion expressed about treatment.

An empyema should be defined as a localised collection of pus in the pleura; it is a mature abscess, the end result of an acute suppurative process. In the early stages there is an acute pleurisy that proceeds to seropurulent effusion; this seropurulent effusion matures, the pus thickens, thickened pleural exudate and limiting adhesions develop (unless the empyema is total) until finally an abscess is formed. In the earlier formative stages the seropurulent fluid is thin and if left in a container will sediment out to give a layer of clear supernatant serous fluid above a deposit of pus. As the process matures the proportion of purulent deposit increases until finally there is little or no supernatant clear fluid. To describe the earlier formative stages of the acute suppurative pleurisy as an empyema is just as wrong as to describe the early stages of an acute septic cellulitis as an abscess before a localised collection of pus has formed. The fundamental importance of paying attention to the stages of development of an acute septic cellulitis in deciding treatment is obvious. It is no less fundamental to consider the stages of development of the suppurative pleurisy in deciding the treatment of empyema. The term "empyema" should cease to be used as synonymous with the whole process of septic pleural infection and should be reserved for the mature condition or residual abscess which results.

In neglected cases, or in those which have become chronic, a thick layer of fibrous tissue is formed over the parietal and visceral pleuræ; this may become a serious factor in preventing re-expansion of the lung and in perpetuating the abscess cavity. In very old, chronic, encysted cases the empyema cavity becomes lined with calcified or even ossified plaques.

An empyema may rupture into a bronchus and be coughed up; this only very rarely leads to spontaneous cure, for usually the drainage is inadequate. Occasionally it will point externally, giving the so-called "empyema necessitatis"; most of such cases are tuberculous in origin. Delayed or inadequate drainage leads to continued toxæmia, or to amyloid disease; there is also a danger of pyæmic complications, especially cerebral abscess.

Symptoms and Signs.—The symptoms are varied and may often be insidious in onset. The simplest clinical picture is that presented by the pneumococcal form, when the temperature either fails to return to normal or when it rises again and assumes the remittent type; the patient, instead

of improving, begins to show signs of a severe toxæmia ; there are pallor, hectic flush, sweating at night, loss of appetite, and wasting. Often, especially in streptococcal cases, the presence of an empyema may be entirely overlooked owing to the severe general illness and absence of any symptoms pointing to such a collection. Many tragedies occur through a misdiagnosis of " unresolved " pneumonia ; it is essential to bear in mind the possibility of an empyema, for only too often a bitter disclosure occurs in the post-mortem room.

The physical signs are the usual ones of pleural effusions, although it is sometimes possible to hear loud tubular breathing through the fluid, more especially in children. High leucocytosis with a relative increase in the polymorphonuclears is valuable confirmatory evidence. Postero-anterior and lateral radiographs of the chest are of great value even if taken in bed when the patient is too ill to be moved. There should be no hesitation in the repeated use of an exploring needle in doubtful cases.

Prognosis.—The condition is always serious, although less so in pneumococcal than in streptococcal infection. Below the age of five it carries with it a high mortality, especially in infants below one year ; in these, however, the empyema is usually only a contributory factor occurring in an illness associated with septicæmia, extensive pneumonia, pericarditis, meningitis, or middle-ear disease. In empyemata associated with pneumonia the mortality is much higher in the cases in which the empyema develops before the pneumonia has resolved ; *i.e.*, syn-pneumonic empyema bears a worse prognosis than meta-pneumonic empyema.

Treatment.—The treatment has been much confused by attempts to introduce complicated methods and by the ignoring of certain fundamental principles. In considering the treatment of a mature empyema it is necessary to consider the treatment of the earlier acutely infected pleura. Failure to understand the pathology of pleural infection is responsible for much of the confused thought and advice that has reappeared with the introduction of chemotherapy, and notably penicillin. The effect and indeed the success or failure of penicillin will be greatly influenced by the stage of evolution of the pleural suppuration. The exhibition in the early " cellulitic " phase is more likely to be followed by successful control of the process than in the later stages when there is an abscess with thick pus, walls covered with tough exudate and often fibrin clots or purulent masses lying in the cavity. Penicillin can kill organisms and often can sterilise the contents of an abscess, but operation is still needed in many cases to correct the secondary mechanical effects of the infection which can prevent healing. Healing in an empyema depends upon expansion of the lung to obliterate the infected pleural space.

The fundamentals of treatment consist of (*a*) assessment of the correct time for drainage, (*b*) provision of adequate drainage, (*c*) institution of proper physical treatment, (*d*) decision as to the correct time to stop drainage.

(*a*) *The Correct Time for Drainage.*—In the early formative stages of pleural suppuration drainage is both unnecessary and dangerous ; unnecessary because with proper management by aspiration and chemotherapy (*i.e.*, penicillin) it may be possible to achieve resolution. It may be dangerous because in this early phase the patient is often suffering from the effects of a severe invasive general infection, often with pneumonia or septicæmia, and may be unable to withstand the extra mechanical strain thrown upon him if a total pyopneumothorax follows ; this is especially true of children and

infants. Aspiration and chemotherapy should be maintained until the pus has thickened to form a mature abscess; by this time the severe invasive phase of the infection has usually also passed. Drainage is rarely safe before the third week unless the presence of a bronchial fistula is causing choking and coughing.

(*b*) *Adequate Drainage.*—Aspiration alone or intercostal drainage alone may cure an empyema, but many of the cures of "empyema" by these methods alone are really cures of early pleural infection. They are often valuable as temporary measures but are never satisfactory when fibrin masses are present, and to persist in their use prolongs the patient's illness and exposes him to the grave risk of a chronic empyema. Drainage by rib resection is needed for proper pleural toilet as well as for the insertion of an adequate sized tube.

(*c*) *Physical Treatment.*—In all empyemata the ultimate object is to obliterate completely the abscess cavity and this is brought about by re-expansion of the compressed lung. The value of proper breathing exercises cannot be too strongly stressed and their effective use should prevent any falling-in of the chest wall and scoliosis, or displacement of the mediastinum and diaphragm which result in permanent deformity and impaired respiratory efficiency. The treatment of an empyema should be ambulatory as early as possible.

(*d*) *When to stop Drainage.*—It is wrong to remove the tube after an empiric or arbitrary time such as two to three weeks. There is only one safe time to remove the tube and that is when a cavity can no longer be demonstrated to exist in the pleura. If the tube is removed before this there is a great risk of a chronic empyema following. Too early removal of the tube is the commonest cause of chronicity. It is essential to study the size and shape of the cavity by means of repeated pleurograms (*i.e.*, radiography after injection of iodised oil) in order to adjust the tube properly and assess the time for its removal.

Arrest of the natural process of obliteration of the empyema cavity results in a *chronic empyema*. In addition to too early removal of the tube this may be due to drainage performed too early (when the lung is totally collapsed), too late (when the walls are too rigid), drainage in a faulty place (too high, too low, or too far forward in the axilla), or to the use of too small a tube. In a number of cases chronicity is due to disease of the underlying lung such as carcinoma, cystic disease, tuberculosis; the condition of the lung must always be carefully assessed in chronic empyema.

When chronicity is not due to underlying lung disease cure is often achieved by establishing good drainage and giving intensive physical treatment. Suction drainage may assist. Decortication is invaluable in selected cases and can result in rapid healing with complete restoration of function. In some cases thoracoplasty may be required.

R. C. Brock.

DISEASES OF THE MEDIASTINUM

Mediastinitis.—Acute pyogenic mediastinitis occurs as the result of the spread of infection from the neck, œsophagus, or trachea, and follows, for example, ulceration due to impacted foreign bodies or to neoplasms. It may also complicate empyema, pericarditis, wounds of the chest, and pyæmia.

Substernal pain, cough, fever, and dyspnœa are outstanding symptoms.

In many cases chemotherapy is worthy of a trial, while staphylococcal antitoxin should also be used in cases due to that organism. Therapy is otherwise surgical, and the prognosis is in any case serious.

Syphilitic Mediastinitis.—This is an increasingly rare disease in which the clinical and radiological appearances may simulate mediastinal neoplasm or aortic aneurysm. The patient complains of cough and increasing dyspnœa. Gummatous ulceration of the sternum and anterior chest wall may have occurred, and thus persistent sinuses may be present. The gummatous mass in the mediastinum, as a rule, obstructs the superior vena cava, causing cyanosis and venous congestion in the head, neck, and arms. The Wassermann reaction is positive, and therapy should at first consist of large doses of potassium iodide, after a prolonged course of which other antisyphilitic treatment may be instituted.

Tuberculous Mediastinal Lymphadenitis (*vide* p. 86).

Mediastinal Neoplasms.—Fluorography will disclose a growth in the mediastinum before anatomical and functional derangement of adjacent organs occurs and long before physical signs and symptoms are apparent. Surgical therapy in many cases is thereby made simpler, more effective, and far less dangerous. Mediastinal neoplasms as a class give rise to symptoms and signs which are for the most part dependent upon pressure on neighbouring structures.

The superior vena cava, or one of its main tributaries, may be obstructed with the production of venous congestion, cyanosis, and œdema in the area concerned. Dilated and tortuous veins are visible on the front of the chest and on the abdominal wall. Through these, blood passes downwards and ultimately reaches the inferior vena cava. Arterial obstruction may cause unequal radial pulses, unilateral clubbing of the fingers, and sometimes thrombosis with gangrene.

Dysphagia results from œsophageal obstruction, and chylous effusion from involvement of the thoracic duct. Pleurisy with or without effusion occasionally arises. Paralysis following a phase of irritation of the recurrent laryngeal, the vagus, the sympathetic, the phrenic, or intercostal nerves may occur.

Pressure on the trachea gives rise to a characteristic " brassy " cough, and later to dyspnœa and stridor, while bronchial obstruction from similar causes provokes somewhat similar symptoms, and in addition may result in atelectasis and secondary suppurative changes in the area of lung affected.

Finally, pressure on bones causes erosion, a constant boring pain, and in the case of the spine ultimately gives rise to paraplegia. Radiological examination, including screening, a barium swallow, and bronchography is of great value in diagnosis. Neoplasms causing these symptoms and signs may be primary or secondary.

Sarcoma and more commonly carcinoma in various primary sites may have mediastinal metastases. It is unusual in cases dying of bronchial carcinoma to find the tracheobronchial or paratracheal mediastinal glands free of neoplastic change.

Innocent primary tumours include retrosternal goitre, thymoma, chondroma, lipoma, endothelioma, neurofibroma, and teratoma. Of these, the last two are, as a rule, situated respectively in the posterior and anterior mediastinum, and, while the thymoma overlies the root of the heart, the retrosternal goitre tends to occupy the superior mediastinum in the thoracic

outlet. Any of these tumours may undergo malignant changes. Treatment is surgical.

Aneurysm of the aorta is not uncommon and is perhaps the best known of the mediastinal tumours (*vide* p. 433). It is worth remembering that the rare isolated congenital dextro-position of the aorta regularly produces dysphagia with the advent of arteriosclerotic change within its walls. Œsophageal pouches and dilatation of the œsophagus, such as that produced by achalasia of the cardia, may give rise to bizarre symptoms and signs referable to other mediastinal structures, while œsophageal neoplasms occasionally are productive of clinical changes of the type recorded above.

Finally, lymphoma (Hodgkin's disease and lymphosarcoma) constitutes a common mediastinal tumour, and very frequently appears to originate in the mediastinal glands (*vide* p. 283).

W. D. W. Brooks.

RENAL DISEASES

RENAL FUNCTION

MIGRATION of primitive forms of life from their original habitat —the sea—to the less stable conditions of fresh water and land, demanded the elaboration of more complex mechanisms whereby the constancy of the internal medium could be maintained independently of changes in the external environment. In particular it was necessary to guard against undue loss, or accumulation, of water and salt. These duties were largely taken over by the kidneys, or other excretory organs, in addition to their primordial function of eliminating waste products. Although elimination is the more obvious function of the kidneys, conservation (*i.e.*, by reabsorption and sometimes selective secretion) is equally important. By means of these two processes—elimination and conservation—the kidneys, together with the lungs, skin, and bowel, regulate the reaction and osmotic equilibrium of the blood and tissues. As part of this regulatory function the kidneys also elaborate ammonia and hippuric acid and are concerned in the breakdown of the more complex ketones.

The vast majority of substances normally eliminated in the urine are brought to the kidney already formed in the blood. Transference from blood to urine alters their relative concentrations but does not change them chemically. Concentration, then, is an essential, and perhaps the most important, feature of excretion by the kidney. For all practical purposes, normal renal function means ability to concentrate to a normal degree, and failure to do so constitutes *impairment of renal function.* Concentrating ability is directly proportional to the number of functioning renal units or *nephrons* (*i.e.*, a glomerulus with its corresponding tubule), of which there are slightly less than one million in each human kidney. Usually only some 20 per cent. of the nephrons are simultaneously active, but under conditions of stress all are engaged. There is, therefore, an enormous *renal reserve.* Not until between two-thirds and three-quarters of the total number of nephrons (total renal substance) is rendered inactive does loss of concentrating ability become manifest. Disease of the kidneys may therefore be quite extensive before diminution of renal function is apparent.

Renal disease and impairment of renal function are therefore not synonymous. Impairment of renal function frequently occurs in a "functional" sense; it is not necessarily associated with structural changes in the kidneys as, for example, when mechanical obstruction to the flow of urine, with increasing back-pressure, gives rise to impairment of renal function, which may return to normal when the obstruction is removed. Renal function, indeed, fluctuates in a surprising manner in response to a large variety of external stimuli, and especially to those that cause temporary alterations in the blood supply to the kidneys, without the ordinary signs of renal disease being present.

Characteristic of the normal kidney is its ability to adapt itself to

changing conditions. Presented with a large quantity of fluid for elimination, it responds by excreting a large volume of dilute urine ; if the fluid intake be restricted, or an excess of water be lost from the body by sweating, vomiting, or diarrhœa, a small volume of highly concentrated urine is excreted. Impairment of renal function may therefore be revealed either by inability to concentrate, or to dilute, according to circumstances. Inability to concentrate is usually evident earlier ; but, with increasing impairment of function, diluting power is inevitably affected, so that eventually it becomes impossible to form either a very dilute or a very concentrated urine. Finally, all elasticity of response is lost, and if any urine at all is excreted it attains a fixed specific gravity of about 1010 (more strictly 1·010). Fixity of the specific gravity of the urine at 1010 (*isothenuria*) is a certain sign of extreme impairment of renal function. It may be noted that 1010 is approximately the specific gravity of the blood serum after removal of the serum proteins.

Deficient concentration in the urine eventually leads to accumulation of urinary constituents in the blood, and diminution of renal function may be revealed in this way also. Such a condition is referred to as *renal insufficiency*, *urinæmia*, or, more commonly, *uræmia*. Renal function may be severely impaired, however, without undue accumulation of urinary constituents in the blood when certain " compensatory " mechanisms are brought into play. The most important of these is *polyuria*. Deficient concentration is for a time compensated for by increased volume ; so that, in a given period, the total quantity of waste products eliminated is sufficient to prevent accumulation. This is known as *compensated impairment of renal function* (Fishberg). Eventually, with progressive loss of function, a stage is reached in which a sufficient volume of urine cannot be elaborated, compensation fails, accumulation occurs in the blood, and a condition of *decompensated impairment of renal function*, i.e., *renal insufficiency*, supervenes. Renal disease, therefore, may or may not be accompanied by, or progress to, impairment of renal function, whilst the latter may not be so severe as to amount to renal insufficiency.

Impairment of renal function affects simultaneously the maximum concentration in the urine in which all the substances normally eliminated can be excreted, though not to the same degree. Even substances which are not normally found in the urine, such as albumin, sugar, and the ketone bodies, are, in the presence of severe impairment of renal function, excreted in diminished concentration. A reduction in the concentration of albumin in the urine is therefore not always a sign of improvement. Ability to excrete water may also be impaired, as shown by a deficient water excretion test (*vide* p. 503). The extent to which the various substances are diminished in concentration in the urine when renal function becomes impaired is roughly proportional to the degree in which they are normally concentrated by the kidneys. This explains why some substances accumulate in the blood in renal insufficiency, whilst others apparently do not. Creatinin and urea, for example, which are normally concentrated some eighty and sixty times respectively in their passage through the kidneys, readily accumulate in the blood when renal function becomes impaired. Uric acid also accumulates in such circumstances, though not so readily, being normally only concentrated some thirty times by the kidneys. Chloride, calcium, sodium, and water, on the other hand, which are normally scarcely concentrated at all

by the kidneys (*i.e.*, their concentration in blood and urine is practically identical), do not accumulate in the blood in renal insufficiency. Phosphate, sulphate, and potassium occupy an intermediate position in this respect. The hall-mark, then, of impairment of renal function is diminution of concentrating power, whilst that of renal insufficiency is retention in the blood. The latter, like the analogous cardiac insufficiency, is a relative term, when, for example, there is nitrogenous retention on a diet containing a normal amount of protein, but not when the protein intake is limited. Impairment of renal function is present all the time, but renal insufficiency only under conditions of greater stress ; or, to put it another way, a decompensated impairment of renal function has become compensated, in this instance, by diminishing the protein intake.

The decompensation of a previously compensated impairment of renal function is one of the most important events in renal disease, and may be brought about in a variety of ways. Thus, since polyuria is by far the most important factor in maintaining compensation, anything which diminishes the volume of urine may lead to decompensation. Urinary volume may be diminished for many reasons, some renal and others extra-renal in origin. The only strictly renal cause of diminished urinary volume (oliguria, or anuria) is a degree of impairment of renal function so severe that the kidney is unable to eliminate a sufficient quantity of water. This is a comparatively rare event. Far more often compensation is broken by extra-renal causes in which water is diverted from the kidneys into the tissues (*pre-renal deviation*), where it becomes " bound " and is consequently not available for excretion. Extra-renal oliguria is seen, for example, in myocardial failure, excessive vomiting or diarrhœa, the rapid formation of general œdema and intercurrent febrile disorders. In general, decompensation may be brought about by (*a*) diminished concentration, (*b*) diminished volume, and (*c*) increased katabolism.

Because urea accumulates most readily in the blood, and its estimation therein is comparatively easy, the blood urea is generally used as an index of renal efficiency. In clinical medicine it is also regarded as indicative of the nitrogen content of the blood and therefore of the degree of *azotæmia*. At first it was believed that, except from increased protein katabolism, the blood urea was only increased when renal function was impaired. Later, it was found that azotæmia frequently occurred in a large variety of disorders in which there was no reason to suspect damage to the kidneys and in which ability to concentrate seemed to be normal. This apparent paradox, referred to in earlier editions of this book as extra-renal, or pre-renal, azotæmia, was believed to be due to a decrease of urinary volume so pronounced that, despite normal concentration, the *output* of nitrogen lagged, and accumulation in the blood resulted. Recent and more delicate tests of renal function (*vide* Inulin and Diodrast Clearances, p. 506) show, however, that in these cases renal function is, in fact, impaired. Extra-renal azotæmia, therefore, differs in degree, but not in kind, from that associated with more obviously diminished renal function. Apart from excessive endogenous protein katabolism, it would seem that azotæmia is generally, if not always, due to impairment of renal function, though it is not necessarily accompanied by demonstrable structural changes in the kidneys (*vide* p. 512).

TESTS OF RENAL FUNCTION

Until recently it has not been possible to assess separately the functional capacity of the two main components of the nephron—the filtering power of the glomerulus, and the reabsorbing (or secretory) ability of the renal tubule. Most methods of estimating renal function have, therefore, been based on the most conspicuous feature of renal activity, namely, ability to concentrate. The earliest tests, indeed, consisted in noting the absence of odour in the urine in renal disease after the ingestion of such substances as asparagus and turpentine, and the delay in the appearance of the colour in the urine after the administration of certain dyes.

As, moreover, all the urinary constituents are more or less simultaneously affected when the concentrating power of the kidney is diminished, it follows that any one, or all, of them may properly be used as an index of renal function. Practical considerations caused urea to be generally selected for this purpose, though there is no inherent reason for this.

So far as the urine is concerned all the necessary information regarding concentrating ability may be obtained by a study of the specific gravity. Impairment of renal function, therefore, may be estimated easily and accurately by following the specific gravity of the urine ; but for the diagnosis of *renal insufficiency* an examination of the blood is essential, and for general purposes an estimation of the urea content of the latter is the most convenient. It has been stated that the total non-protein nitrogen, the creatinin, and the uric acid contents of the blood give earlier evidence of the approach of renal insufficiency. It is doubtful whether such claims can be upheld, and certainly in practice the advantages are negligible.

Great care is necessary in interpreting the results of any method of estimating renal function. Severe renal disease frequently leads to serious disturbances in other systems and organs, and it is upon these that the ultimate prognosis often depends. While, therefore, renal function tests afford fairly accurate information as to the extent of the local lesion, if used as an index of the general prognosis they must be considered in relation to the whole clinical state.

At one time or another almost all substances which are capable of excretion by the kidney, and which can be readily estimated in the blood and urine, have been used as an index of renal function. The number of renal function tests is therefore very large. It is only possible here to describe two of the most valuable in any detail—the Specific Gravity and the Urea Clearance Tests. To facilitate reference brief comments are added on some of the more important of the other tests, but for details of their application larger works should be consulted.

Tests from a Study of the Urine.— *Appearance.*—Babylonian physicians of 4000 B.C. were interested in the colour and perhaps composition of the urine. In the Middle Ages inspection of the urine was sometimes carried out by professional uroscopists. Later, the diagnosis was made by the physician, after inspection of the urine, but treatment was carried out by the apothecary (Kilduffe). Taken in conjunction with the clinical findings much information may be obtained from noting the appearance, and particularly the colour, of the urine. With normal renal function a small volume of urine will usually contain much pigment and have a high specific gravity. Absence

of pigment with a small volume of urine and a low specific gravity generally indicates severe impairment of renal function. The intensity of the pigmentation of two simultaneous specimens obtained by ureteric catheterisation will often give information as to the relative functional capacity of the two kidneys, even before chemical analysis has been carried out. In general, when much fluid is either lost from the body entirely, or diverted to the tissues in the form of œdema, the urine is highly coloured, and of high specific gravity, if renal function is normal. On the other hand, if large quantities of fluid are being consumed, or œdema fluid and serous effusions are being absorbed, the urine may be colourless and of low specific gravity with quite normal renal function, but the volume will be large.

Specific Gravity of the Urine.—The specific gravity, interpreted with regard to the conditions obtaining at the time, will often supply all the information required concerning the functional capacity of the kidneys. To determine to what extent impairment of function has given rise to accumulation in the blood, direct analysis of the latter must be made.

In general, the specific gravity of the urine varies inversely as the volume, the extreme range in health being from about 1002 to 1040, with an average of 1015 to 1020. The night urine is usually more concentrated than that passed during the day.

Information of value may sometimes be obtained by a consideration of the specific gravity alone, even in a single and casual specimen ; for if in the absence of a large quantity of protein or sugar it be high, *i.e.*, 1026 or more, renal function is probably intact whatever the volume of urine excreted. With values lower than this no assessment of renal function can be made without a knowledge of the corresponding volume. The close inverse relationship which normally exists between urinary specific gravity and volume forms the basis of the Concentration and Dilution Tests.

The Concentration (Specific Gravity) Test.—After complete abstention from fluids for a period of not less than sixteen hours (beginning on the previous evening) the specific gravity of three consecutive hourly specimens of urine is estimated. If renal function is normal, then at least one of the readings will be 1022 to 1035, or even 1040, though values below 1025 must be regarded with suspicion and the test should be repeated. The specific gravity of small volumes of urine may be estimated by the use of Specific Gravity Beads, but if less than 3 c.c. is available it is easier to estimate the concentration of urea, which under these circumstances should be not less than 2 per cent. No correction is required for less than 4 parts per 1,000 of protein. For 4 parts subtract 001, 8 parts 002, 12 parts 003, and 16 parts 004 from the observed specific gravity reading. The concentration test should be performed before the dilution test when both are required.

The Dilution (Specific Gravity) Test.—Water to the amount of 1,200 c.c. (or 42 oz.) is drunk in the course of half an hour, the patient being in bed. The bladder is emptied at *hourly* intervals for four consecutive hours after this, and the specific gravity of each specimen (which, for reasons explained later, is also carefully measured) is taken. If renal function is normal, then at least one of the readings should be below 1010, and may even reach 1002. Values above 1008 should be regarded with suspicion.

Water Excretion Test.—In four hours a normal subject, who has taken no food or drink for the preceding twelve hours, will eliminate approximately the whole of 1,200 c.c. of water taken in the course of half an hour, the larger

part being excreted in the first two hours, and for this reason the hourly specimens of urine obtained in the course of carrying out the Dilution Test are accurately measured. If, owing to deficient renal function, water elimination is impaired, then probably less than 800 c.c. will be excreted in four hours. There are, however, many other causes of impaired water elimination, *i.e.*, those of pre-renal deviation (*vide* p. 501). A poor water-excretion test, therefore, may be due to reasons other than diminished renal function. If, however, poor water excretion is associated with a normal concentration test, then impaired water excretion is of extra-renal origin. *Per contra*, if diminished water excretion is associated with a poor concentration test, the former may be due to either renal or extra-renal causes.

The Urea Concentration Test (Maclean and de Wesselow).—After abstaining from fluid for twelve to eighteen hours the bladder is emptied completely. Fifteen grammes of urea in 100 c.c. are then drunk and the bladder again emptied at hourly intervals for three hours. If renal function is normal the concentration of urea should be not less than 2 per cent. in at least one of these specimens. If the volume of any hourly specimen exceeds 150 c.c. it is of no value for the test and should be discarded. This test is of value only as a rough indication of renal function.

Excretion Urography.—In addition to its value for outlining the renal tract under X-rays, this procedure (*vide* p. 543) will give information of the excretory power of the kidney. After the intravenous injection of an iodine-containing contrast medium a good shadow of the renal pelvis should be obtained in five minutes. Delay in the appearance of this shadow or its absence indicates defective renal excretion.

Analysis of the Blood as an Index of Renal Function.—Analysis of the blood provides evidence that urinary constituents are present therein in excess, but does not show whether such excess is due to renal or to extra-renal causes. Urea, the total non-protein nitrogen, creatinin, uric acid, and phosphate are often estimated, but for all practical purposes the blood urea furnishes all the information required.

The Blood Urea.—Normally the blood contains from 20 to 40 mg. of urea per 100 c.c. In the very young and in normal pregnancy 20 to 25 mg. per 100 c.c. may be regarded as the upper limits of the normal. In the aged up to 50 mg. per 100 c.c. may also be considered normal. The extent to which urea may accumulate in the blood in renal insufficiency depends upon several factors, among which are: the severity and duration of the renal inadequacy, the efficiency of compensatory mechanisms, the fluid intake, the protein content of the food, the rate of protein katabolism, and the functional capacity of the liver which elaborates urea. Urea, being an easily diffusible non-electrolyte, is found in practically the same concentration in most of the tissues of the body and therefore may be estimated in either plasma, serum, or whole blood, cerebrospinal fluid, and, with suitable precautions, in saliva. By appropriate measures (*vide* p. 513) a raised blood urea due to renal insufficiency may be reduced to normal, though the patient may die from "uræmia."

Simultaneous Tests on Blood and Urine for the Estimation of Renal Function.—Ambard, as a result of simultaneous studies of the concentration of urea in the blood and urine, laid the foundations for most of the subsequent work on renal function tests.

The Addis Ratio.—Addis found that when the kidney is working to its

maximum capacity after being " loaded " with the administration of a large dose of urea and extra fluid, the ratio

$$\frac{\text{milligrams urea in one hour's urine}}{\text{milligrams urea in 100 c.c. blood}}$$

is proportional to the number of functioning nephrons. He showed that this ratio is really a measure of the volume of blood cleared of urea by the kidneys in one hour, and thus introduced the conception of the " clearance " tests.

The Blood-urea Clearance Tests.—Moeller, McIntosh, and Van Slyke developed the conception of blood-urea clearance to include not only that amount of blood which was cleared of urea in a given time when the kidney was working to maximum capacity, but for conditions in which renal capacity was not fully taxed. According to these workers the kidney is always working to its maximum capacity when urine is excreted at the rate of about 2 c.c. per minute or more. Under such conditions the rate of urea excretion is directly proportional to the concentration of urea in the blood, and the volume of blood which is cleared of urea in one minute is termed by Van Slyke the *maximum clearance.* In health this is relatively constant at about 75 c.c. When the rate of urine excretion is less than 2 c.c. per minute, the amount of blood cleared per minute is not constant, but varies as the square root of the urinary volume. This is termed the *standard clearance*, and averages about 54 c.c. The maximum and standard clearances can therefore be derived from the two following formulæ, which are applied respectively according to whether the rate of urinary excretion is above or below 2 c.c. per minute :—

$$\text{Maximum clearance or } C_m = \frac{UV}{B}$$

$$\text{Standard clearance or } C_s = \frac{U\sqrt{V}}{B}$$

where U = urinary urea in milligrams per 100 c.c.
B = blood urea in milligrams per 100 c.c.
V = volume of urine in cubic centimetres per minute.

The authors give the following normal values for adults :—

Maximum clearance range 64 to 99 c.c. mean 75 c.c.
Standard clearance range 40 to 68 c.c. mean 54 c.c.

It is necessary to make a correction for surface area in the case of children and for adults of abnormal stature.

For comparative purposes it is convenient to convert the results into percentages. This can be done by multiplying the maximum clearance and the standard clearance figures by 1·33 and 1·85 respectively.

Expressed as a percentage of the normal, values below 75 indicate renal deficiency. Symptoms of " uræmia " are said to appear with values below 5 per cent., but not above 10 per cent. It is important to note that values below normal may be due not only to disease of the kidney itself but also *to diminished renal blood flow*, e.g., *heart failure.* Repetition of the test in the same subject will often show considerable variations in the result.

The test is carried out as follows. Between breakfast and lunch (tea but not coffee may be taken with breakfast) the bladder is emptied and the

specimen is discarded. *Exactly* sixty minutes later (a stop-watch should be used) the bladder is again emptied, and the resulting specimen is *accurately* measured (in cubic centimetres and not in ounces) and its urea content determined. The bladder is again emptied exactly sixty minutes later and the specimen measured and its urea content determined as before. A sample of blood is taken for estimation of the blood urea at the end of the first hour. If the volume of urine exceeds 2 c.c. per minute the maximum clearance is calculated ; if less than this, the standard clearance, by means of the formulæ given. It is important that the bladder be *completely* evacuated on each occasion and that the volume of urine be accurately measured. In subjects with marked renal deficiency the test should be performed in the recumbent position. In actual practice many observers find that the standard clearance does not always give satisfactory results, and recommend that the maximum clearance be used. In order to ensure that the kidney is working to full capacity it is customary, immediately the bladder has first been emptied, to give a dose of 15 to 20 gm. of urea in 300 c.c. of water, and to give a further 300 c.c. of water at the end of the first half-hour. Even with these precautions a fairly high proportion of subjects, especially those with renal or cardiac disease, fail to give a sufficient diuresis for the satisfactory application of the test. It is, of course, unnecessary to give urea when the blood urea is already known to be over 80 or more milligrams per 100 c.c. A further difficulty arises, as it is never certain that the bladder has been completely emptied, and routine catheterisation is certainly not justified.

The urea clearance test is regarded as the most sensitive test of renal function at present available, but its successful performance demands the most meticulous attention to details. It gives valuable information in the hands of those skilled in its use and interpretation.

In assessing results it is important to remember that urea clearance varies directly with renal blood flow, which, of course, alters from minute to minute. Within a certain range, therefore, variations in clearance are evidence of normal response by the kidney. This normal range is from 75 to 130 per cent. of the average normal. Values over 75, therefore, represent normal renal function ; from 75 to 50 are considered doubtful ; and if factors causing " functional " uræmia (*vide* p. 514) can be excluded, values below 50 indicate impairment of renal function.

Inulin and Diodrast Clearance Tests.—The principle of the clearance test has been applied by Homer-Smith and others with conspicuous success to the separate estimation of glomerular and tubular functions. For this purpose the inert polysaccharide inulin and the organic iodine compound diodrast are substituted for urea. Inulin being neither secreted nor reabsorbed by the tubular epithelium can be used to ascertain the rate of glomerular filtration, while diodrast, which is excreted mainly by tubular secretion, gives a measure of tubular function. Simultaneous estimations of inulin and diodrast clearances have revealed degrees of impairment of renal function not shown by the use of the less sensitive renal function tests which have been described above. Thus in benign essential hypertension a considerable degree of impairment of renal function can be demonstrated by the use of inulin and diodrast clearances, which is not apparent with either the urea clearance or the specific gravity (concentration) tests. In their present form the technique of the inulin and diodrast clearance tests is too elaborate

for routine use. For details of their application the original papers should be consulted.

Alkaline Tide and Renal Function.—In some forms of Bright's disease the alkaline tide diminishes or disappears. Under suitable circumstances this fact may be used as an early indication of impairment of renal function. Thus, if the reaction (*p*H) of the pre- and post-breakfast specimens of urine be charted daily in a series of cases of scarlet fever, the diminution or disappearance of the alkaline tide will readily be seen when renal function becomes impaired, and this may occur some days before the appearance of frank signs of renal disease such as albuminuria or hæmaturia. In fact, it is sometimes possible to forecast the occurrence of post-scarlatinal or post-tonsillitic nephritis in this manner.

SIGNS AND SYMPTOMS OF RENAL DISEASE

Albuminuria.—Leube (1878) first showed that persistent albuminuria occurs in some 5 to 10 per cent. of otherwise normal men. This albuminuria appeared to be without pathological significance and without undue liability to develop Bright's disease. This was apparently confirmed in army recruits during the war of 1914-18 by Maclean and de Wesselow. The more recent work of Dublin, however, on the after-histories of a large number of insurance applicants rejected on account of albuminuria, indicates a more guarded prognosis. A thorough clinical examination, together with renal function tests repeated at intervals, will help to differentiate between a true benign albuminuria and one having pathological significance. The presence of more than a few red blood cells or casts on several occasions is strong evidence of an active renal lesion.

It has long been known that even in normal urine small numbers of casts and red and white blood cells are present. Addis has evolved a quantitative method for the estimation of these elements, which is known as the Addis Sediment Count. The technique is difficult, but the method is of value in differentiating between benign and pathological albuminuria, and is indispensible for the adequate control of the apparently healed, though still active, phase of a recovering acute nephritis. Addis gives the following figures from investigations on healthy subjects, which he expresses as rates of excretion in the twelve-hour night urine :—

	Average.	Variations.
Casts	1,040	0 to 4,270
Red blood cells	65,750	0 to 425,000
White blood cells and epithelial cells	322,550	32,400 to 1,000,000

In a doubtful case of albuminuria a persistent and marked excess of any or all of these elements would point to the presence of an active renal lesion.

Orthostatic Albuminuria (*Adolescent, Postural, Lordotic, Cyclical Albuminuria*).—A variety of albuminuria is found in some 15 to 30 per cent. of children and adolescents, especially those of nervous temperament and poor development. It is characterised by the small quantity of albumin present, and the readiness with which this disappears with rest. It is believed to have no pathological significance and no specific treatment is required. Dublin's figures suggest a tendency for such adolescents to

develop pulmonary tuberculosis. Claims that the normal albumin-globulin ratio is reversed in this condition do not seem to have been substantiated.

Symptomatic Albuminuria,—Albuminuria is met with in a great variety of physiological and pathological conditions. Thus it invariably accompanies prolonged violent exertion, as in football or rowing, especially in the untrained, and may be caused by cold baths and emotional stress. It also frequently occurs with acute infections of all kinds, especially when pyrexia is present, and in passive congestion of the kidneys in heart failure, and after convulsions, as in epilepsy. These conditions will also cause temporary fluctuations in the degree of albuminuria due to frank renal disease.

Hæmaturia.—The appearance of abnormal numbers of red blood corpuscles in the urine. Blood may appear in the urine as the result of injury or disease of any part of the urinary tract or adjacent organs, and in a few diseases of other parts of the body. The chief causes of this symptom may be conveniently summarised as follows :—

1. Hæmorrhage from the kidneys :
   - (*a*) Inflammatory : acute nephritis, tuberculosis, pyelitis.
   - (*b*) Malignant hypertension — essential benign hypertension (" Renal Epistaxis ").
   - (*c*) Traumatic : calculus, oxaluria, injury.
   - (*d*) Growth : malignant—hypernephroma, carcinoma, sarcoma.
     benign—papilloma, angioma, and capillary nævus of pelvis.
   - (*e*) Blood Diseases : purpura, scurvy, hæmophilia.
   - (*f*) Drugs : turpentine, carbolic, hexamine, luminal, sulphonamides.
   - (*g*) Congenital cystic kidney, hydronephrosis, aberrant renal vessels.
   - (*h*) Embolism and infarction.
2. From the ureter : ureteric calculus—papilloma.
3. From the bladder : papilloma, carcinoma, acute cystitis, tuberculosis, bilharzia, engorgement of vesical veins from adenoma or carcinoma of prostate, calculus, injury.
4. From the urethra : trauma, acute urethritis, calculus.
5. From disease originating outside the urinary organs : extension of abscess from prostate, appendix, pelvis, psoas abscess, pyosalpinx : carcinoma of uterus, rectum, cæcum, sigmoid and pelvic colon : tuberculous ulceration of small intestine, and diverticulitis.
6. Contamination from other sources : menstruation, cervicitis, balanitis.

Occasionally hæmaturia may occur without demonstrable cause and apparently without sequelæ. This has been designated " essential " hæmaturia. A similar idiopathic hæmaturia occasionally occurs in families.

Hypertension.—The close association between hypertension and kidney disease has long been known. It led to the belief that hypertension was always, or generally, due to renal disease. The discovery by Mahomed (1874) that hypertension often occurred without albuminuria suggested, however, that it also arose from extra-renal causes. Two varieties were thus recognised : one secondary to frank renal disease—renal hypertension ; the other not associated with renal disease and due to unknown causes—

" primary," or " essential," hypertension. A puzzling feature of the latter was the almost invariable presence at autopsy of more or less conspicuous vascular changes (especially of the afferent arterioles) in the kidneys. Since these changes were often very slight, and the hypertension was known to have been present for many years, it was assumed that they were the result of the hypertension, and not its cause.

This dual conception of the origin of hypertension held the field until 1934, when Goldblatt *et al.* succeeded in producing persistent hypertension in dogs by *partial* constriction of the renal arteries with metal clamps. Wilson and Byrom (1939) then showed that constriction of one renal artery in rats resulted in persistent hypertension without changes in the clamped kidney (which was " protected " by the clamp), whilst vascular lesions (fibrinoid necrosis and endarteritis), characteristic of malignant hypertension in man, developed in the unclamped (unprotected) kidney as well as in all the other organs commonly affected in this disorder. It was proved that whilst renal ischæmia causes hypertension, the latter, in turn, induces destructive vascular lesions in the kidneys and elsewhere. A vicious circle is thus set up. A similar sequence is believed to be the explanation of the progressive course of many types of chronic renal disease.

These experiments, however, do not explain by what mechanism renal ischæmia causes hypertension. It is probable that experimental (constrictive) hypertension is caused by chemical means and not through the agency of the nervous system as it develops even after preliminary sympathectomy or destruction of the spinal cord. The search for the responsible pressor agent was long and mainly unsuccessful, although Tigerstedt and Bergmann (1898) had already described a powerful pressor substance which they had extracted from the cortex of normal kidneys, and which they named Renin. Their work, however, failed to excite much attention until recently when the isolation and properties of renin have been the subject of intensive study.

The mode of action of renin is complicated but may be summarised thus : it is a protein extracted only from the renal cortex. It behaves as an enzyme, and causes vaso-constriction only in the presence of another constituent of normal blood (renin activator : prehypertensin or preangiotonin) which is associated with the pseudoglobulin fraction of the blood. Prehypertensin is probably produced in the liver, but only when the adrenal cortex is functioning normally. Renin reacts with prehypertensin (which becomes used up) to produce a third substance—hypertensin (angiotonin), the effective pressor substance. Finally, hypertensin itself is destroyed by another enzyme—hypertensinase (antirenin), which is found in normal kidney and in other tissues.

It can scarcely be doubted that experimental (constrictive) hypertension is due to liberation of renin from an ischæmic kidney ; but that this mechanism is the cause of persistent hypertension in man is not yet proved. There is, however, much experimental evidence to suggest that the hypertension of benign and malignant essential hypertension, as well as that of chronic glomerular nephritis, may have a similar origin.

Hypertensive Retinopathy (Retinitis).—Retinal lesions, apart from œdema, are rare in renal disease except as a manifestation of hypertension. They occur in two main forms : (1) *hypertensive neuro-retinopathy* and (2) *arterio-sclerotic retinopathy*. Since neither inflammation nor albuminuria is directly

concerned in the pathogenesis of either form, the terms "retinitis" and "renal" or "albuminuric" retinitis are inapplicable and should not be used.

1. Hypertensive neuro-retinopathy occurs in those forms of Bright's disease associated with marked and persistent hypertension. It is met with, therefore, in chronic glomerulo-nephritis, chronic pyelonephritis, malignant hypertension, and toxæmia of pregnancy. The early stages of neuro-retinopathy may occasionally be seen in acute glomerulo-nephritis but they commonly regress. The chief ophthalmoscopic findings are: (*a*) slight swelling and redness of the disc with blurring of its margins, and these are often the earliest signs; (*b*) a greyish fogging of the retina beginning at the disc and fading towards the periphery; (*c*) the appearance of white spots ("cotton-wool" or "snow-bank" spots) of fatty and œdematous change in a wide area surrounding the disc, which later become transformed into glistening white or yellow, sharply defined, opaque spots similar to those found in arteriosclerotic retinopathy; (*d*) linear, round, flame-shaped or irregularly shaped hæmorrhages; (*e*) *narrow*, brightly striped ("silver wire"), but not conspicuously tortuous arteries, and dilated and engorged veins. Many factors combine to produce these changes of which the chief are: (i) vaso-constriction of the retinal arterioles; (ii) acute necrotising arteriolitis; and (iii) increased intracranial pressure. The very varied ophthalmoscopic picture presented in different patients and in different stages of the several diseases is mainly due to the relative preponderance of one or other of these underlying factors. More than a moderate swelling of the disc (*i.e.*, choked disc), for example, implies considerable increase of intracranial pressure so that malignant hypertension, either as a primary condition or as complicating an antecedent nephritis, may be diagnosed almost with certainty. Hypertensive neuro-retinopathy is invariably present in malignant hypertension, occurs in from 30 to 50 per cent. of cases of chronic glomerulo-nephritis, and is frequently met with in toxæmia of pregnancy when it is specially liable to cause detachment of the retina. Although the lesions of hypertensive neuro-retinopathy sometimes cease to progress with temporary improvement in the renal disease, the prognosis (except in pregnancy toxæmia) is generally grave, few surviving for more than two years after the first appearance of retinal changes.

2. Arteriosclerotic retinopathy also occurs in patients suffering from prolonged hypertension, though not (except in diabetes) in arteriosclerosis of the larger vessels without hypertension. It is generally met with, therefore, in benign essential hypertension, though it is often seen in chronic glomerulo-nephritis with or without hypertensive neuro-retinopathy. The main features of this form of retinopathy are: (*a*) irregularity in the calibre of the retinal arterioles; (*b*) *thickening* of the arterial walls; (*c*) arterio-venous compression; (*d*) increased tortuosity of the vessels; (*e*) absence of œdema of the disc; (*f*) retinal hæmorrhages, linear, rounded or irregular in shape, few, or many; (*g*) numerous hard, shiny, white or yellow spots, often clustered in a stellate pattern in the region of the macula. Soft, "woolly" spots do not occur. It may be noted that narrowing of the retinal arterioles is a sign of vaso-constriction, not of arteriosclerosis. In the latter the vessels tend to be thickened and therefore wide. Histological examination has shown that arteriosclerosis of the retinal vessels may be present before ophthalmoscopic evidence is apparent. Although arteriosclerotic retinopathy is essentially a bilateral condition the characteristic retinal picture may be

confined to one side for long periods in a high proportion of the cases. Occasionally ischæmic atrophy of the disc results. The prognosis is, of course, determined by that of the primary condition so that it is usually not good. On the other hand, this form of retinopathy, unlike hypertensive neuro-retinopathy, is often compatible with many years of fair health.

ŒDEMA

Dropsy, though still a prominent symptom in many of the principal forms of Bright's disease, does not dominate the clinical picture in civilised communities to the extent that it did at the time Bright wrote his classical papers. It is still, however, a prominent feature in nephritis occurring in under-nourished races. From this it may be inferred that, whatever the precise pathogenesis of œdema in nephritis, its development is favoured by an underlying state of malnutrition and all that that may imply. Œdema in Bright's disease may be considered under three headings — cardiac, nephritic, and nephrotic, and its treatment is discussed in the appropriate sections (*q.v.*).

It should be remembered that œdema of the lower extremities may result from many causes other than renal or cardiovascular disease. These include severe anæmia, pelvic tumours, thrombo-phlebitis, cachexia of all types, and nutritional diseases. In addition, a moderate bilateral œdema of the feet and ankles of uncertain origin is not uncommon in women. This type of œdema has apparently no pathological significance, though it may be unsightly and inconvenient.

Cardiac Œdema.—Cardiac œdema is of frequent occurrence in those forms of Bright's disease characterised by arterial hypertension, *i.e.*, in primary granular kidney and in chronic glomerular nephritis. Heart failure in these conditions is a common event, and is generally the immediate cause of death. In some cases of acute nephritis the heart gives way in face of a sudden increase of blood pressure, and a cardiac œdema is superimposed upon a nephritic œdema. Cardiac œdema may generally be recognised by accompanying signs of back-pressure such as dyspnœa, cyanosis, and enlargement of the liver, and by the appearance of œdema in the dependent parts. It is essentially due to increase in the capillary blood pressure, but the deficient circulation also injures the capillary wall, as shown by the moderate increase in the protein content of the œdema fluid, which is generally about 0·5 per cent. Estimation of the blood cholesterol is sometimes of value in differentiating between a cardiac and a nephrotic œdema. An increase in the blood cholesterol (above about 220 mg. per 100 c.c.) is suggestive of the latter.

Nephritic Œdema.—Nephritic œdema is not primarily due to circulatory embarrassment and is less influenced by gravity. Posture therefore plays only a secondary part in its distribution. Nephritic œdema typically begins in the face, though later it may extend to the whole body. Often, however, in patients who are ambulatory, œdema is first noticed in the feet or ankles. The cause of nephritic œdema is believed to be an increased permeability of the capillaries throughout the body, which permits the escape of water and proteins into the tissue spaces. The protein content of the œdema fluid is therefore high, generally over 1·0 per cent.

Nephrotic Œdema.—Nephrotic œdema does not differ from nephritic œdema in its clinical characteristics or distribution. It is due to diminished colloid osmotic pressure of the plasma proteins, caused mainly by continued loss of proteins into the urine. The protein content of the œdema fluid is low and generally under 0·1 per cent. It is met with in nephrosis, the nephrotic stage of glomerular nephritis, and in amyloid disease of the kidney. It also results from diminution of the plasma proteins from extra-renal causes, *i.e.*, without loss of protein in the urine, as from malnutrition in hunger œdema, and in the gross ascites of cirrhosis of the liver, in which large amounts of protein are withdrawn from the blood. It will be noted that of the three forms of œdema commonly met with in cases of renal disease, two, namely, cardiac and nephritic œdema, are entirely extra-renal in origin. Only one, nephrotic œdema, is caused chiefly by renal disease. These three types of œdema may occur singly or combined, so that the pathogenesis of œdema in renal disease is often exceedingly complex.

AZOTÆMIA AND URÆMIA

The term "uræmia" (or "urinæmia") was originally used to describe the symptom complex that was believed to result from the intoxication of blood imperfectly purified by the kidneys; in other words, poisoning with urine. Before it was realised that many of the signs and symptoms of Bright's disease occurred independently of renal insufficiency, it was customary to attribute them all to this cause. Thus, the numerous hypertensive symptoms of Bright's disease, especially those of hypertensive encephalopathy (*vide* p. 593), became included under the heading of uræmia. The term is now restricted to those signs and symptoms which *directly* and *invariably* accompany the retention of urinary constituents in the blood *as a result of renal insufficiency*. In spite of the fact that none of the known constituents of the urine, alone or together, is directly capable of reproducing any of the clinical manifestations of this state, it is exceedingly useful to retain the term, as defined, in clinical medicine.

It will be recalled (*vide* p. 500) that the expression "renal insufficiency" is used to denote uncompensated impairment of renal function. It follows that uræmia must be accompanied by azotæmia (increased nitrogen content of the blood). Until recently it was believed that azotæmia often occurred without renal insufficiency, and even with normal renal function—so-called "extra-renal" azotæmia or uræmia (*vide* p. 501). It would now seem that azotæmia generally occurs only as a result of renal insufficiency and that the term "extra-renal," used in this connection, is misleading. Both azotæmia and uræmia, therefore, are essentially renal in origin. Azotæmia may, of course, occur without clinical uræmia when renal insufficiency is not sufficiently severe to give rise to symptoms. Both azotæmia and uræmia may be associated with structural changes in the kidneys, or may occur without such—functional azotæmia and uræmia. Functional uræmia may conveniently be considered separately because, although it differs only in degree, and not in kind, from uræmia associated with structural changes in the kidneys, it generally arises from very different causes. It is important to remember that functional uræmia may be added to an existing uræmia associated with structural changes in the kidneys, and thus increase the gravity of the latter.

Symptoms of Uræmia.—The symptoms of uncomplicated uræmia are best seen when mechanical obstruction to the flow of urine is present, because for a long period the symptoms are not obscured by those of an added hypertension. For this reason they are more often observed by the surgeon than the physician. They are :—

1. Mental and physical fatigue, weakness, drowsiness, and dullness that suggests narcosis. The physical fatigue may be extreme, quite intolerable, and may dominate the clinical picture.
2. Excitation phenomena : involuntary coarse muscular contractions, especially of extensor groups, increased tendon and skin reflexes, contraction of the pupils, deep breathing, and hiccoughs.
3. Alimentary disturbances, such as anorexia, vomiting, and diarrhœa.
4. Rapid loss of weight and emaciation.
5. Severe hypochromic anæmia and non-thrombocytopenic purpura.
6. Tendency to inflammation and necrosis, pharyngitis, laryngitis, stomatitis, gastritis, enteritis, necrotic ulcers of the mouth, stomach, intestines, and colon, and often pericarditis.
7. Urinary smell in the breath.
8. Subnormal temperature.
9. Cardiac irregularities—usually dropped beats, sometimes preceding sudden death.

Asthenia is the most constant symptom. It is important to realise that severe headache and convulsions are not a feature of true uræmia but of an associated hypertensive encephalopathy. None of these symptoms is usually conspicuous until the blood urea is about ten times its normal value. Sudden and unexpected death occurs in about 5 per cent. of patients dying from uræmia. It is generally, but not always, associated with an excessive accumulation of the potassium ion in the blood.

Treatment of Uræmia.—Before beginning treatment it is necessary to differentiate clearly between the symptoms of uræmia (*i.e.*, the syndrome resulting from renal insufficiency) and those of hypertensive encephalopathy because the two conditions so frequently occur together, especially in chronic Bright's disease. Since there are no direct means of improving renal function the treatment of uræmia consists essentially in diminishing the accumulation of waste-products in the body. This is achieved firstly by increasing the output of urine and secondly by limiting the diet. Treatment should be controlled by estimations of the blood urea at least every few days.

When there is neither intractable vomiting nor coma the fluid intake should be increased to not less than 4 (and not much more than 5) pints by mouth in twenty-four hours. If diuresis sufficient to diminish the blood urea does not result, the low protein diet described on page 523 should be given as well. Diuretics other than alkaline salts are contraindicated. An alkaline mixture containing 30 to 60 gr. of sodium bicarbonate and potassium citrate in equal parts may be given by mouth (or as a 3 per cent. solution per rectum or intravenously) to combat acidosis and to stimulate diuresis when increasing the fluid intake and dietetic measures fail. Alkaline therapy, however, should never be attempted unless it is controlled by repeated estimations of the alkali reserve and the potassium content of the blood. When such facilities are not available it is safer to give normal, or slightly hypertonic (2 or 3 per cent.), saline or 5 per cent. glucose intravenously.

Some degree of *heart failure* often occurs in uræmia and for this digitalis may be given, and frequently results in increasing the output of urine. *Tetany*, also, often complicates uræmia, and for this calcium chloride (1 gr. in 30 minims of water or saline) may be given intramuscularly and may be repeated, or calcium gluconate and parathormone (*vide* p. 216) may be tried.

Theoretically the extra-renal elimination of waste-products should be encouraged, but in practice such methods as purgation, diaphoresis, and venesection are ineffective and even harmful, and should be avoided. When, however, uræmia is associated with hypertensive encephalopathy, venesection may be required (*vide* p. 593). Blood transfusion is always contraindicated.

Intractable vomiting may sometimes be controlled by gastric lavage, cocaine ($\frac{1}{4}$ gr.) by mouth, or morphia. *Pruritus* may be relieved by ergotamine ($\frac{1}{2}$ to 1 mg., t.i.d.) by mouth, bromides, or morphia. *Persistent hiccough* may be controlled by re-breathing into a closed paper bag, or morphia may be required.

For *restlessness and insomnia* any of the usual sedatives may be used, since none has any peculiar advantages in uræmia. All must, however, be given with caution since the kidneys are unable to excrete any excess.

Sudden, unexpected (and unexplained) *death* occurs in about 5 per cent. of all cases of severe uræmia (excluding functional uræmia), and it is important to warn relatives of this possibility.

Functional Uræmia.—This condition, formerly known as " extra-renal " uræmia, is met with in a very large number of widely different disorders, among the more important of which may be cited :—

1. Vomiting, severe and protracted from any cause, but especially in high intestinal obstruction, hyperemesis gravidarum, and in the vomiting which accompanies uræmia in Bright's disease (*i.e.*, a " functional " uræmia may be superimposed upon a non-functional uræmia).
2. Intestinal obstruction without vomiting, but with retention of fluid in the intestinal tract—acute dilatation of the stomach.
3. Diarrhœa, severe and prolonged, from any cause.
4. Gastro-intestinal hæmorrhage (severe)—hæmatemesis or melæna.
5. In " shock," whether due to trauma, surgical operations, associated with extensive burns, or in cardiac infarction.
6. Acute liver disease—acute hepatic necrosis and the so-called hepato-renal syndrome.
7. Diabetic ketosis.
8. Addison's disease.
9. Fevers.
10. Sepsis—empyema, peritonitis, etc.
11. Heart failure.
12. Peripheral circulatory collapse—associated with any of the above or with other disorders.
13. Alkalosis—as in the alkaline treatment of peptic ulcers.

The clinical features are often difficult to define, since they are apt to be overshadowed by those of the accompanying, or primary, disorder. Irritability, depression, and insomnia, and an unpleasant and sometimes " metallic " taste, are common and early symptoms. Lassitude and lethargy, leading to stupor and coma, are also frequently present. There may be a

dull headache, but severe headache and convulsions do not occur. Involuntary muscular twitchings, vomiting, diarrhœa, pruritus, and urinous odour in the breath have all been observed but are not common. The symptoms, in fact, are those of mild uræmia as seen in urinary obstruction and in Bright's disease, though unlike the latter they are not usually complicated by those of hypertensive encephalopathy.

Azotæmia is as a rule moderate in degree, the blood urea being from 50 to 100 mg. per 100 c.c., though values of 400 and 500 mg. per 100 c.c. are occasionally met with. Owing to the frequency with which persistent vomiting accompanies the causal condition the azotæmia is apt to be associated with an alkalosis and a hypochloræmia. Since, too, the causal condition is generally associated with loss of fluid from the body (vomiting and diarrhœa), or its diversion into the tissues (œdema formation), marked oliguria often occurs. The specific gravity of the urine is generally high, though, relatively to the small volume, it is below normal, loss of concentrating ability being thus masked. Formed elements and albumin do not appear in the urine until the condition has been present for some days, when slight albuminuria and a few red blood cells and casts are apt to appear. Absence of these qualitative signs of renal disease in the early stages also obscures the renal origin of the azotæmia. Functional azotæmia differs from the non-functional variety in another respect—the high concentration of urea in the urine in the former. This is due to the increased protein katabolism which occurs in so many of the causal disorders.

Many theories have been advanced to explain the mechanism by which renal function becomes impaired in the absence of structural changes in the kidneys. By far the most important factor which influences renal function from moment to moment both in health and in disease is the amount of blood flowing through the kidneys. Diminution in the total quantity of blood in circulation must mean a diminished return to the heart, a fall in cardiac output, and a diminished blood flow through all the organs of the body. For a time the more vital organs, the heart and brain, will maintain (through arteriolar constriction) their blood flow at the expense of less immediately important organs such as the kidneys. In functional uræmia, however, it is not the heart which fails first but the peripheral circulation. Peripheral circulatory collapse (known clinically as "shock") is a conspicuous feature of all conditions causing functional uræmia. Functional uræmia is therefore caused by "shock." Prognosis and treatment likewise are the same as in "shock." What ultimately causes shock is another question (*vide* p. 419).

Anuria.—Anuria may be divided into four main ætiological groups: (i) Pre-renal, (ii) Renal, (iii) Post-renal, and (iv) Combined Group. The chief *pre-renal* causes are: inadequate fluid intake or excessive fluid loss, *i.e.*, vomiting, diarrhœa, and severe hæmorrhage; shock and any of the causes of functional uræmia (*vide* p. 514); reflex anuria, *e.g.*, catheterisation or calculus. *Renal anuria* is met with in acute nephritis and toxæmia of pregnancy; advanced chronic nephritis, pyelonephritis, hydronephrosis, bilateral cortical necrosis; acute necrotising nephrosis (burns and poisoning with heavy metals). *Post-renal anuria* is mainly due to urinary obstruction from any cause, whilst the anuria of blackwater fever, incompatible blood transfusion (*vide* p. 262), the crush syndrome, traumatic uræmia, and that which occurs in sulphonamide therapy are due to a combination of tubular

obstruction and tubular degeneration. It will be seen later, however, (p. 517) that the most important feature of this form of anuria is renal anoxia.

Treatment of Anuria.—Anuria is more liable to arise when the kidneys are previously diseased. Careful preliminary examination and selection of patients before instituting treatment likely to cause anuria, *e.g.*, surgical operations, anæsthetics, and blood transfusions, are therefore important preventive measures. Treatment of the underlying cause often relieves anuria so that specific measures should be deferred until the anuria has persisted for at least forty-eight hours.

Fluids should always be given by mouth when possible, or even per rectum, in preference to the intravenous route. It is first necessary to determine whether the anuria is associated with (*a*) severe dehydration and (*b*) an acidosis or an alkalosis. Dehydration can usually be assessed on clinical grounds. When present the fluid intake should be not less than 5 to 6 pints per twenty-four hours. When there is no obvious dehydration the fluid intake need not exceed 4 pints. Anuria is usually associated with an acidosis, but alkalosis may accompany severe and persistent vomiting or prolonged hyperpnœa. Except when alkalosis is present or suspected the alkaline mixture described on page 546 should be given by mouth at hourly intervals (or when necessary as a 3 per cent. solution per rectum) until either the *rate of urine excretion* is at least 30 to 40 oz. per twenty-four hours (ascertained if necessary by passing a catheter at six-hourly intervals), or symptoms of intolerance (tetany) develop. In the latter event treatment must be abandoned. When an adequate diuresis occurs the quantity of alkali should be reduced by increasing the intervals between doses at first to two hours, then three hours, and so on, provided a satisfactory rate of urine excretion is maintained. If this method fails, or alkalosis is already present, a solution of 5 per cent. glucose should be given intravenously at the rate of 50 drops per minute (*i.e.*, 6 pints in twenty-four hours). Acid salts (*i.e.*, ammonium chloride) should not be given to combat alkalosis.

Sodium citrate and bicarbonate should be substituted for potassium citrate in the above mixture when the potassium content of the blood is likely to be already above normal, *e.g.*, in the renal insufficiency of chronic Bright's disease and in the crush syndrome. Treatment of anuria with alkalis should always be controlled by estimations of the bicarbonate content of the blood. Renal decapsulation is sometimes advocated for anuria but its value has not been established. When conservative measures fail, high (4th dorsal segment) bilateral splanchnic nerve block should be tried. Mercurial diuretics are strongly contraindicated in any form of anuria.

The Crush Syndrome.—Aerial bombardment during the war led to many instances of persons being pinned beneath fallen masonry for many hours. A frequent result is compression of a limb, with consequent necrosis and autolysis of striated muscle, and liberation of large amounts of myohæmoglobin and potassium into the blood and urine. Apart from the local trauma, and symptoms of hæmorrhage and shock, the main clinical feature is a marked and progressive oliguria accompanied by myohæmoglobinuria and numerous pigmented casts in the urine, leading to complete anuria, azotæmia, and death from uræmia. The renal tubules, especially the ascending limb of Henle's loop and the second convoluted tubule, are largely obstructed by the pigmented casts containing myohæmoglobin, though the anuria is also

in part due to damaged renal epithelium. Treatment consists in giving alkaline salts (sodium citrate and bicarbonate, not potassium salts), preferably by mouth, otherwise by intravenous drip.

Traumatic Anuria and Traumatic Uræmia.—Fatal anuria and uræmia also occur after severe war wounds and extensive injuries from industrial accidents in which limb compression and muscle necrosis are not evident. The pathogenesis is obscure though, as in the crush syndrome, the main lesion is in the renal tubules. Treatment is as for the crush syndrome.

Renal Anoxia.—A feature common to many forms of anuria, especially those associated with the crush syndrome, traumatic uræmia, incompatible blood transfusions, and cortical necrosis, is anoxia of the renal cortex resulting from local vasoconstriction. The brilliant experiments of Trueta and his colleagues have shown that sympathetic stimulation leads to vasospasm of the cortical vasculature with the result that the blood is diverted from the cortex through the vessels of the medulla. If this essentially temporary and, in a sense, protective reaction is unduly intense or prolonged, anuria will result. This suggests that the correct treatment for cortical anoxia is either to endeavour to tide the patient over the period in which the cortex is excluded from the circulation, and waste-products are therefore accumulating in the blood, by the use of Kollf's "artificial kidney" or peritoneal dialysis, or by doing a splanchnic block. There is, indeed, clinical evidence that these measures have all at times proved successful in the conditions named, and doubtless their efficacy will increase with experience in their use. In desperate circumstances they should be tried.

BRIGHT'S DISEASE

In 1827 Dr Richard Bright of Guy's Hospital pointed out that coagulable urine and dropsy were often associated with disease of the kidneys. Thereafter such conditions were known as Bright's disease. It later became apparent that many different pathological states were included under this heading, so that the expression Bright's "diseases" is more accurate. It is customary and convenient to retain the term as a group-name for certain non-suppurative renal disorders, chief among which are: all forms of nephritis, nephrosis, and nephrosclerosis, and their cardiovascular sequelæ; chronic pyelonephritis; the renal complications of pregnancy and diabetes; and such conditions as amyloid disease of the kidney and renal dwarfism. Recent work on renin (*vide* p. 509) suggests also that most instances of "essential" hypertension should be restored to the family of Bright's diseases, from which they were removed following the work of Mahomed some seventy years ago.

Bright's disease, in one or other of its numerous forms, is probably the most common cause of death in this country, and its morbidity greatly exceeds the recorded mortality. At autopsy it is found in a gross form more than twice as often as it is diagnosed in life. A large, though as yet undetermined (estimates vary from 40 to 70 per cent.), proportion of disorders masquerading in official lists as heart disease is mainly renal in origin and should appear under the heading of Bright's disease.

Despite the more dramatic appeal of cancer and tuberculosis, Bright's disease is the most important medical problem of the day.

No completely satisfactory classification of the various forms of Bright's

disease has yet been evolved. A simple and practical scheme is to divide them into three main groups as follows :—

(i) Nephritis.
(ii) Nephrosis.
(iii) Primary Nephrosclerosis.

Nephritis (Syn. : Acute and Chronic Diffuse Glomerular, or Glomerulo-tubular, Nephritis). Nephritis may be defined as a " bilateral non-suppurative inflammatory disease of the kidneys " (Osler), and occurs in four forms :—

(i) Diffuse glomerulo-nephritis (acute, subacute, and chronic).
(ii) Focal non-embolic glomerulo-nephritis.
(iii) Focal embolic glomerulo-nephritis.
(iv) Acute interstitial " nephritis."

DIFFUSE GLOMERULO-NEPHRITIS

In all forms of nephritis the three main structures of the kidney—the vasculature (including the glomerular tuft), the tubules (including Bowman's capsule), and the interstitium—are simultaneously or successively involved. Glomerulo-nephritis is so called to emphasise that the initial lesion occurs in the glomerular tuft (Klebs, 1876). The adjectives diffuse and focal are used to distinguish between two forms of the disease—the former in which all, or most, of the glomeruli are simultaneously affected from the outset, and the latter, in which only a few glomeruli, or even only occasional loops of some of the tufts, are involved.

In its most typical and complete form diffuse glomerulo-nephritis is characterised by three stages : acute, subacute, and chronic. The corresponding anatomical terminology for these stages is : the blood-dripping kidney ; the large white kidney (one form of) ; and the secondary contracted or small white kidney. Clinically they are known respectively as acute nephritis, subacute or nephrotic nephritis, and chronic nephritis. It is worth emphasising that the term " chronic nephritis " applies strictly to the third or chronic stage of diffuse glomerulo-nephritis, and to no other form of Bright's disease.

Often the disease passes through each successive stage—sometimes rapidly (two months from onset to death in the third stage) and sometimes very slowly (twenty years or longer). The relative duration of each stage varies enormously, and transition from one stage to the next may be comparatively abrupt or almost imperceptible. In spite of these diversities the leading features of each stage are relatively distinct and the diagnosis is not usually difficult. Frequently the disease becomes arrested at the acute stage, and occasionally after the subacute stage. Very often the acute stage is so mild that it escapes recognition, and the patient is first seen with well-marked signs and symptoms of the subacute or chronic stages. In others, many months or even years after apparent recovery from the acute stage, signs and symptoms of the chronic stage are noticed, the subacute stage being missed. The long silent interval between the acute and chronic stages is sometimes referred to as the *latent stage* of glomerulo-nephritis.

Much more frequently than is generally realised a large number of various infections is accompanied and followed by a low-grade glomerulo-nephritis, revealed only by careful and repeated examinations of the urine. Unsuspected or *subclinical nephritis* of this kind is an important cause of "idiopathic" chronic glomerulo-nephritis. Generally speaking, however, the three main stages of diffuse glomerulo-nephritis are so distinct that it is convenient to describe them separately.

ACUTE GLOMERULO-NEPHRITIS

(*Acute Nephritis*)

Acute nephritis probably always results from a previous infection elsewhere in the body, though cold and exposure are devitalising and therefore predisposing causes. In some 80 per cent. of cases in civilians it follows a streptococcal infection of the tonsils or other parts of the upper respiratory tract; its incidence is therefore greatest in childhood. Scarlet fever was the foremost cause, but of recent years the incidence and severity of this disease has much diminished, and it now accounts for only a very small proportion of the total number of cases of acute nephritis. Other infections, such as pyodermia, pneumonia, infected wounds, malaria, and influenza, are occasional causes. It is curiously rare in erysipelas. Acute nephritis (diffuse form) also sometimes accompanies rheumatic fever, purpura, and subacute bacterial endocarditis.

Age Incidence.—The age incidence is that of the primary infection, and the disease is therefore most frequent in childhood and early adolescence.

Sex Incidence.—At all ages acute nephritis is more common in males, roughly in the proportion of three to two, and this is attributed to the greater likelihood of exposure. There is evidence that this disparity in the sex distribution is becoming less marked.

Familial Incidence.—Acute nephritis occurring in several members of a family, either simultaneously or at intervals, is not very uncommon, but it is doubtful how far this is coincidence and how far it is due to familial predisposition.

Epidemics.—Epidemics of acute nephritis were observed during the American Civil War, the war of 1914-18, when it was known as "trench nephritis," and the influenza epidemic of 1929. Post-scarlatinal glomerulo-nephritis is more common in some years than in others.

Exposure and Chill.—Exposure and chill, especially associated with a wetting, have long been regarded as important causes. There is little doubt that they act as predisposing causes of infection, and in this manner give rise to acute nephritis.

Morbid Anatomy.—The kidneys are usually normal in size, or large, soft, congested, and drip blood—the "blood dripping" kidney. The capsule strips easily. On section there is good differentiation between cortex and medulla, and the glomeruli may stand out as pale greyish or dark red points. *Microscopically* the initial lesion is an endocapillaritis of the capillary loops of all the glomeruli, which are swollen, occluded, and empty of blood. This is followed by proliferation of the endothelium of the loops and the appearance of polynuclear leucocytes within the glomerulus, and the whole

tuft becomes enlarged. The walls of the glomerular loops undergo hyaline degeneration, individual loops often fusing. Albuminous exudate and red cells escape into the capsular space. The cells of the tubules in this stage often show little change, slight cloudy swelling, or fatty degeneration. The lumen of the tubules may contain blood, albumin, and casts. The arteries also often show little change at first, though later a necrotising arteriolitis of the afferent arterioles and thrombosis may be found. In cases which do not resolve, thickening and hyalinisation of the glomerular loops occur after a few weeks or months and the capsular epithelium proliferates, forming the characteristic "epithelial crescents." The case has then entered the subacute stage. It will be observed that the fundamental lesion in the kidneys in acute nephritis is a diffuse endocapillaritis, *i.e.*, it is primarily a disease of the vascular system. The tubules are only secondarily involved, mainly as a result of diminished supply of blood from the corresponding diseased glomerulus.

Pathogenesis.—The renal lesions in acute nephritis are not due to the presence of the infecting organism in the kidneys, for they are rarely found there, but to the injury set up by circulating toxins. This injury, however, is not a direct one due to bacterial toxins, for nephritis does not generally arise until some time after the initial infection and more often than not during convalescence, *i.e.*, long after the concentration of circulating bacterial toxins has diminished. This latent interval is of much importance in a consideration of the pathogenesis of the disease. In analogy with the latent interval in serum sickness, and because of other evidence, both clinical and experimental, it is thought that the renal lesions are due to a hypersensitive state developed during the acquisition of immunity. For example, acute diffuse glomerulo-nephritis frequently occurs in the course of subacute bacterial endocarditis, not during the active septicæmic stage but later during a bacteria-free stage. This constitutes the "allergic" theory of the pathogenesis of acute nephritis. Another theory is that acute nephritis is but the local manifestation of a generalised capillary disease. This is supported by the fact that œdema frequently occurs so early and may precede the albuminuria, and that the high protein content of the œdema fluid suggests injury and increased permeability of the capillaries all over the body. Finally, microscopical examination of the capillaries of the nail-bed in acute nephritis has shown tortuosity and thickening of these vessels. Volhard interprets the ischæmia of the afferent glomerular capillaries in the early stages of acute nephritis as evidence of local vascular spasm, and regards the hypertension, narrowing of the retinal vessels, and pallor of the skin as evidence of a generalised vascular spasm (Volhard's Angio-spastic Theory). Hypertension, however, is not invariably present, nor are the capillary loops always completely devoid of blood. The view now mostly held is that the characteristic changes in the kidney and in the arterioles throughout the body in acute diffuse glomerulo-nephritis represent the reaction of these tissues to the overproduction of immune bodies which constitute the noxious agents or "toxins" concerned.

Clinical Picture.—The clinical picture and course are extremely varied. The urinary changes, cardiovascular signs, or œdema may dominate the picture, alone or in any combination, either throughout or at different stages of the disease. The signs and symptoms of the primary infection may overshadow those of the nephritis. The course, too, is varied and may be

rapid or slow. The onset likewise may be sudden or insidious. Fulminating cases also occur. Nearly always there is a latent interval between the primary infection and the appearance of signs and symptoms of nephritis.

Hæmaturia and œdema are usually the first clinical signs, but either may occur alone or precede the other by some days. Puffiness of the eyelids in the morning is a common initial symptom, often followed by swelling of the feet, legs, and external genitalia within a few days. The urine may be bloody and scanty and there may be frequency, urgency, and lumbar pain or aching. Vomiting and abdominal pain with high temperature are common in children, and occasionally in them the attack begins with acute cerebral symptoms, such as headache and convulsions. In some instances the onset is insidious : there is no obvious hæmaturia but some swelling of the ankles is noticed, perhaps after a walk, which later increases and spreads to other parts of the body. In more severe cases the œdema becomes generalised and involves the serous cavities, the lungs, alimentary canal, causing vomiting and diarrhœa, and the brain, resulting in the headaches and convulsions of hypertensive encephalopathy. Urinary abnormalities, perhaps discovered on routine examination, may constitute the whole picture, but usually frank hæmaturia occurs at the outset and then diminishes in quantity, the urine assuming a smoky tint and finally becoming normal in appearance. Red blood cells, however, persist on microscopical examination for weeks or months after the urine appears normal to the naked eye. Albuminuria is constantly present throughout the course of the disease, and varies considerably in quantity, which, however, is only roughly proportional to the severity of the condition. The volume of urine is always diminished at the outset and may only amount to a few ounces in the twenty-four hours. This oliguria is, however, chiefly extra-renal in origin and the specific gravity of the urine is usually high. Complete anuria at the onset, and continued for more than three or four days, is of bad omen, though it does not necessarily indicate a fatal issue. Casts of all kinds, including blood and epithelial casts, are present in the early stages. They vary considerably in number from time to time and, if much blood is present, diligent search may be required to find them.

The blood pressure is usually increased at least in the early stages. In mild cases, however, there may be no hypertension. As a rule the blood pressure becomes normal in the course of two or three weeks and before the other manifestations of the disease have disappeared. It is not sufficiently realised that the heart is almost invariably affected, even in mild cases. Modern methods show enlargement of the heart in the earliest stages, due partly to acute left ventricular dilatation and slight hydropericardium. Left ventricular hypertrophy may appear in from four to five weeks. Bradycardia sometimes develops. In other cases mild myocardial insufficiency is shown by tachycardia, palpitations, dyspnœa, and inability to lie on the left side. Death from sudden heart failure, especially in children, is not exceedingly rare and may be quite unexpected. In other cases heart failure may rapidly develop following a convulsion or attack of vomiting with acute pulmonary œdema, cyanosis, and orthopnœa. Hypertensive encephalopathy may develop at any stage during which the blood pressure is elevated, though it is rare at the onset. Convulsions are less common now than formerly and are only occasionally fatal.

Renal function, as measured by ordinary tests, is often quite normal

even in severe cases with gross œdema and marked hypertension. Death from uræmia is a rare event in the early stages, and generally renal function does not become seriously impaired until the case enters the sub-chronic or chronic stages. The nitrogen retention, which is so often found in the early stages, is mainly due to increased protein katabolism. The blood count is generally normal and, despite the pallor, anæmia is rare in the early stages. Frank retinopathy is rare, but some narrowing of the retinal vessels and small retinal hæmorrhages are not uncommon.

Diagnosis.—The only conditions likely to cause difficulty in diagnosis are an acute exacerbation of a chronic nephritis, focal nephritis, subacute bacterial endocarditis, and periarteritis nodosa. Gross enlargement of the heart in the absence of symptoms of heart failure suggests an acute exacerbation of an underlying chronic nephritis. Œdema, hypertension, or impairment of renal function are inconsistent with a diagnosis of either focal nephritis or the glomerular embolisation of subacute bacterial endocarditis, but typical diffuse glomerulo-nephritis progressing to chronic nephritis frequently complicates the later stages of subacute bacterial endocarditis. Hæmaturia may for a time be the most striking manifestation of acute nephritis. When this is so it is important to bear in mind other causes of hæmaturia, such as tuberculous kidney and neoplasms.

Course and Prognosis.—In a series of 5,000 cases followed over a period of years it was found that some 60 per cent. recovered completely in the course of a few weeks or months ; the majority in six to eight weeks from the onset. The longer recovery is delayed, the less likely is it to be complete, though even after five or ten years, with persistent but mild urinary signs, eventual recovery is not very uncommon. Some 40 per cent. did not recover within two or three months of the onset. About 12 per cent. developed chronic nephritis either with or without passing through a more or less well-defined second or subacute stage ; 11 per cent. progressed to a form of chronic nephritis with azotæmia but without hypertension, sometimes referred to as " aplastic Bright's disease " ; 10 per cent. developed persistent hypertension without other signs of renal disease ; and 7 per cent. continued to pass large quantities of albumin in the urine indefinitely, without other signs of nephritis, a condition known as " leaky kidney." Death during the acute stage is rare, and occurs in less than 5 per cent. of cases. Generally, when there is a definite history of a preceding infection, the onset is brusque, hæmaturia is a prominent symptom, and the ultimate prognosis is good. When there is no history of a previous infection the onset tends to be insidious, œdema is more conspicuous than hæmaturia, and the prospect of recovery is very much less. Some maintain that these two varieties are distinct diseases, but numerous mixed and transitional types occur so that all that can be said with safety is that in general, and especially in children, the more bloody the urine at the onset the better the outlook. The tendency to chronicity is greater in the nephritis following tonsillitis and other infections than in post-scarlatinal nephritis. Acute nephritis developing after the active stage of subacute bacterial endocarditis generally becomes chronic. Nephritis in non-thrombocytopenic forms of purpura in young persons has a particularly bad prognosis. In all cases of acute nephritis extreme oliguria is dangerous, and anuria persisting for more than four days is often fatal. Acute myocardial failure with pulmonary œdema is the most common cause of death, and pneumonia and hypertensive

encephalopathy are the next most common. The amount of œdema, hæmaturia, or albuminuria bear no relation to the immediate or ultimate prognosis. The chances of complete recovery, however, are inversely proportional to the length of time required for any one of these symptoms to abate. This is particularly true with regard to hypertension, though, of course, hypertension may be entirely absent in some patients who eventually die from uræmia. Uræmia, however, is a comparatively rare cause of death in acute nephritis. Age at onset is an important factor. The older the subject at the onset of the nephritis, the less likely is complete recovery, largely owing to the increasing tendency for hypertension to develop and to persist with age.

Treatment of Acute Diffuse Glomerulo-nephritis

Prophylaxis.—The incidence of acute nephritis is as high in those who have previously had their tonsils removed as in those who have not. Tonsillectomy, therefore, is useless as a prophylactic measure. Neither is there evidence that the early use of anti-scarlatinal serum reduces the incidence of post-scarlatinal nephritis. To attain this object the only effective measures are prolonged confinement to bed, combined with the administration of sufficient alkali by mouth (Pot. Cit. and Sod. Bic. in equal parts) to render the urine persistently as alkaline as, or a little more alkaline than, the blood, *i.e.*, *p*H greater than 7·4. It is possible that similar measures applied to patients with tonsillitis would result also in diminishing the incidence of post-tonsillitic nephritis ; but unfortunately this is not always practicable. Sulphonamide therapy has not been proved to diminish the incidence of acute nephritis as a complication of acute infections. Its use in established nephritis is generally contraindicated. Penicillin has no effect on the course of any form of Bright's disease, but incidental infections are exceptionally dangerous in all of them. For the treatment of such infections penicillin is often invaluable. It may also be used with advantage prophylactically in the form of lozenges or chewing-gum for recurrent sore throats in the course of nephritis, but the danger of producing " resistant " organisms must be borne in mind.

General Management.—Strict confinement to bed is imperative in the earlier stages, chiefly to limit muscular activity but also to secure warmth and the avoidance of chills. The fluid intake and urinary volume should be accurately measured and recorded every twenty-four hours, together with an estimation of the specific gravity of a sample of the twenty-four hours' urine. Methods of producing profuse sweating, such as hot air-baths, hot packs, and the injection of pilocarpine, are contraindicated. No purges of any kind should ever be given. Regular action of the bowels should be maintained by simple lubricants such as liquid paraffin, or soap and water enemata.

Dietary.—In early and severe cases absolute starvation, as recommended by Volhard, *i.e.*, no fluids and no solids, should be enforced for three or four days. Experience has shown that patients suffer surprisingly little discomfort under this drastic treatment if a little orange juice be given to moisten the mouth. In less severe cases half a glass of lemonade with added glucose is given thrice daily, and half an orange night and morning. After the first three days this is increased to a pint of lemonade or orange juice *per diem*, with added glucose and some cooked fruit. Thereafter the fluid intake is

regulated to correspond with the previous twenty-four hour volume of urine, and solids are given as follows :—

Early morning—sweetened drink.
Breakfast—fruit, cooked or raw.
Lunch—potatoes with *fresh* butter, compote of fruit.
4 P.M.—fruit, cooked or raw.
Dinner—as lunch.

This diet is a considerable aid to lessening hypertension, œdema, albuminuria, and especially hæmaturia. It is an adequate maintenance diet, albeit dull, for a patient confined to bed and should be continued if possible until any or all of the aforementioned symptoms have abated and show no further daily improvement. Thereafter the diet should gradually be increased by the addition of substances having the lowest sodium content—eggs, boiled fish, chicken, etc. It will be noted that neither milk nor bread are included in this diet, because of their relatively high sodium contents. Proprietary salt-free " salt " should not be used unless it is specified as not containing sodium. Return to a full diet must depend on the patient's subsequent progress but should not be unduly delayed.

Drugs.—No diuretics of any kind should ever be used in the early stages of acute nephritis, though potassium citrate, in doses sufficient to render the urine persistently alkaline, is a valuable aid to recovery if used at the right time. It should never be given in the presence of macroscopic hæmaturia, but should be exhibited as soon as the urine becomes free from blood to the naked eye and provided there is then no serious degree of impairment of renal function.

Surgical Treatment.—Decapsulation is sometimes practised for persistent anuria. There is no satisfactory evidence that it does good, and the operation is rightly falling into disuse. Generally, little can be done in anuria, but the intravenous injection of *hypertonic* solutions (30 c.c. of 30 per cent. NaCl or 30 c.c. of 50 per cent. glucose) may be tried—in addition, of course, to local measures such as hot poultices over the loins. Tonsillectomy should never be carried out during the early stages of acute nephritis, and rarely even later with the object of improving the renal condition or preventing relapses or progression to the chronic stage. The results of tonsillectomy on the subsequent course of acute nephritis are definitely disappointing. Operations designed to relieve sinus infections are also generally of little benefit to the renal condition.

Treatment of Special Symptoms.—The blood pressure should be taken at least thrice weekly in all cases, owing to the danger of comparatively sudden cardiac failure. Should the blood pressure be rising rapidly, immediate venesection should be done. The tendency is to remove too little blood, and less than 20 oz. in an adult is usually ineffective. Digitalis may be given but its value is doubtful. Hypertension does not contra-indicate its use. Hypertensive encephalopathy should be treated by immediate and generous venesection, followed, if necessary, by lumbar puncture. Uræmia is treated as described on page 513.

Duration of Confinement to Bed.—There are so many patients in whom slight amounts of albumin and a few red cells persist in the urine for months and years that it is manifestly impossible to urge strict confinement to bed until all signs of the disease have disappeared. As a general rule, strict

rest in bed should be maintained *until no single sign or symptom shows evidence of further improvement over a period of one month*, if possible including in the signs and symptoms the alkali reserve of the blood plasma and the sedimentation rate of the red blood corpuscles. Certainly, until the two latter have returned to normal, the patient cannot be regarded as having regained a normal state of health, even in the absence of any signs of renal disease, and until then should not lead a full and normal life. The process of getting up from bed should be gradual and carefully watched. A return or exacerbation of any one sign or symptom, lasting for more than forty-eight hours, should mean a further period of strict rest in bed. The best guide in regulating the amount of exercise and the diet in the sub-clinical stage of recovery is a periodical Addis sediment count (*vide* p. 507). Convalescence in the country and residence in dry, warm climates serve less as a direct stimulus to recovery of the local lesion than as an aid to overcoming long and tedious, though necessary, hospitalisation. In this respect it may indirectly improve the renal condition.

After-care.—The after-care in acute nephritis is much the same as that advocated in healed or latent pulmonary tuberculosis, namely, adequate rest, avoidance of chills, and prompt return to bed for some days upon the slightest signs of any infection. The urine should be tested at regular intervals for albumin for several years ; and during this time, if the patient is not in obviously good general health, it is a wise precaution to keep the urine alkaline by taking sufficient potassium citrate daily by mouth as a precaution against relapses due to intercurrent infections. The sedimentation rate should be estimated at first at monthly and then at quarterly intervals.

SUBACUTE GLOMERULO-NEPHRITIS

(Syn. : Second or Nephrotic Stage ; Nephrotic Nephritis ; Chronic Parenchymatous Nephritis ; Large White Kidney ; Myelin Kidney)

Subacute nephritis is a transitional stage between the first (or acute) and the third (or chronic) stages of diffuse glomerulo-nephritis. In its most typical form it is characterised by gross albuminuria and œdema without macroscopic hæmaturia, hypertension, or impaired renal function. Often, however, it is represented only by urinary signs (latent nephritis) following an incompletely recovered acute stage or by one of the residual forms mentioned on page 522.

Ætiology.—When traceable the ætiology is that of the acute stage.

Morbid Anatomy.—The kidneys are large, pale, soft, and often congested. The capsule strips easily, and on section there is good differentiation between cortex and medulla. The cut surface is greasy and flecked with yellow areas of pseudo-fatty or lipoid degeneration (myelin kidney). Microscopically, the chief changes are—increased tubular degeneration with evidence of epithelial proliferation and regeneration, particularly in the formation of numerous epithelial " crescents " ; increasing glomerular obstruction largely due to the crescents ; and the evidence of early fibrosis in the interstitium. A few completely hyaline glomeruli are found but they are not yet shrunken. Vascular changes are not conspicuous though hyaline thickening of some of the afferent arterioles may be seen. Similar but more marked changes

are seen in later phases (called by some "early" or "sub-chronic" nephritis) and these merge imperceptibly into the characteristic histological picture of chronic glomerulo-nephritis (secondary contracted kidney).

Clinical Picture.—The typical clinical (and biochemical) picture is identical with that of primary chronic nephrosis (*vide* p. 534). The terms "nephrotic syndrome," "nephrotic stage," or "nephrotic nephritis" are sometimes applied to this stage. In spite of its superficial resemblance to primary nephrosis there are important differences. Thus a history of a preceding acute stage, or of an attack of hæmaturia, is not uncommon in subacute nephritis. Either would, by definition, exclude primary nephrosis. Again, the eventual appearance of hypertension or impairment of renal function is almost the rule in subacute nephritis but very rare in primary nephrosis. For some years, therefore, it may not be possible to make a correct diagnosis.

Prognosis.—Progression to chronic nephritis is the general rule. There is evidence, however, that recovery is not so rare as was formerly supposed, even when urinary signs have persisted for as long as ten years after the onset of the acute stage. Since an interval of some years may elapse before either unequivocal signs of chronic nephritis (hypertension or impairment of renal function) appear or recovery takes place, it is important not to leave the patient without hope. As at this stage the physician is often unable to forecast the outcome with certainty, it is preferable in practice to substitute the expression *unresolved* (*acute*) *nephritis* for the term subacute nephritis which has acquired a perhaps not quite justifiable connotation of inevitable doom.

Treatment.—When gross œdema and albuminuria are the dominant features the treatment is that described for chronic nephrosis on page 535. When there is no œdema and only urinary signs are present, prolonged rest in bed, a full and varied diet, moderate doses of alkaline salts, and moral encouragement are all required. Later, graduated exercises and selection of a suitable occupation are essential. The degree and duration of bed-rest, exercise, and general management can only be assessed by continuous supervision and the careful study of clinical and laboratory data collected at *regular* intervals and graphed.

CHRONIC GLOMERULO-NEPHRITIS

(Syn.: Chronic Nephritis; Chronic Hæmorrhagic Nephritis; Chronic Interstitial Nephritis (one form of); Glomerulo-nephritis (third stage of); Secondary Contracted Kidney; Small White Kidney)

Ætiology and Occurrence.—It is now believed that chronic glomerulo-nephritis always arises from a preceding attack of acute glomerulo-nephritis. The latter either clears up entirely or progresses to the chronic stage (*a*) after passing through one of the forms of the subacute stage already described, or (*b*) after *apparent* recovery (latent stage), or (*c*) from a previously unsuspected subclinical glomerulo-nephritis (*q.v.*). The factors which determine chronicity are mainly unknown. Chronic nephritis would seem to be more likely to follow tonsillitis than scarlet fever. Acute glomerulo-nephritis, with an insidious onset without a definite preceding infection and chiefly

characterised by œdema without gross hæmaturia as an initial symptom, is also more liable to become chronic. Macroscopic hæmaturia persisting undiminished for more than about six weeks is also a bad prognostic sign with regard to chronicity. On the other hand, the tendency to become chronic is not related to the severity of the acute attack. The age at the onset of the acute attack, however, does exert an influence on the liability to chronicity, which is more marked in older subjects, except in the aged, when the acute disease often runs a particularly benign course. Chronic nephritis occurs at all ages, but chiefly in early life and under thirty-five years of age. It is more prevalent in the male sex, as is the acute disease.

Pathological Anatomy.—The typical kidney of this stage is small and granular (small white kidney, secondary contracted kidney). It is hard and has a thickened capsule which does not strip readily. The granulations are fine and of a pale yellowish colour, which contrasts with the darker coloured shrunken areas surrounding them. On section the cortex is narrow and irregular, and large areas of fibrosis and lipoid degeneration occur. Demarcation from the medulla is poor. The vessels are markedly thickened. There is an increase of the peripelvic fat.

Microscopic Appearances.—There is marked proliferation of the interstitial connective tissue. Arteriolar lesions are prominent and consist mainly of endarteritis obliterans and medial hypertrophy. In long-standing cases arteriolosclerosis and necrotising arteriolitis may also occur. In the later stages (secondary contracted kidney) the histological picture is an advanced stage of that just described, in which hyalinisation and fibrosis of glomeruli, atrophy of tubules, and increase of the interstitial tissue reach enormous proportions. Evidence of epithelial proliferation is lost or is confined to small scattered areas.

Symptoms.—The presenting symptoms are many and varied and include headache, visual disturbances, asthma, anorexia, anæmia, polyuria, œdema, hæmaturia, epistaxis, and dyspnœa. These, together with evidence of hypertension, impairment of renal function and the characteristic urinary changes, make up the clinical picture of chronic glomerulo-nephritis. When all or many of these signs and symptoms are present, the diagnosis is usually not difficult. When one or two predominate for a long period, diagnosis may not be easy.

The exceedingly complex clinical picture of the chronic stage of diffuse glomerulo-nephritis can be most satisfactorily interpreted by realising that all or most of the individual signs and symptoms arise not directly from a diseased kidney but indirectly from at least three more or less independent pathological processes each of which is initiated in the diseased kidney. These processes behave as independent, though often simultaneously operating, vicious circles. Thus the only direct evidence of renal disease in chronic glomerulo-nephritis, or indeed in any form of Bright's disease, is afforded by changes in the urine—oliguria, diminished concentrating ability, albuminuria, hæmaturia, and cylindruria. Other signs and symptoms arise indirectly from either (*a*) hypertension—which in turn causes cardio-vascular changes, retinopathy, amaurosis, epistaxis—and the cerebral manifestations known as hypertensive encephalopathy ; or (*b*) impairment of renal function—which gives rise to azotæmia, polyuria, asthenia, anorexia, muscular twitchings, tetany, pruritus, anæmia, acidosis, and dyspnœa ; or (*c*) albuminuria—with consequent hypoproteinæmia, œdema, and headaches.

One or other of these vicious circles is present in most varieties of Bright's disease, but only in chronic glomerulo-nephritis are all three commonly operating simultaneously over a long period. Although these three fundamental pathological processes arise and may operate independently, in combination they influence one another. Thus the cerebral consequences of hypertension are undoubtedly aggravated by cerebral œdema due to the albuminuria-hypoproteinæmia syndrome, as in acute nephritis and eclampsia. Again, œdema frequently disappears on the supervention of impairment of renal function and azotæmia. Hypertension, also, whilst on the one hand facilitating glomerular filtration, also causes increased renal ischæmia and ultimately renal failure. The symptoms, course, and duration of chronic glomerulo-nephritis, in fact, depend largely upon the intensity and the mutual influence of these three processes.

Individual Signs and Symptoms.—*Hypertension.*—It cannot be too strongly emphasised that hypertension is not an invariable symptom of chronic nephritis. In many patients the disease runs its full course to a fatal termination in uræmia without hypertension occurring at any stage. In the majority, however, hypertension appears sooner or later and often dominates the picture. When this happens, death from gradual myocardial failure often occurs and may be foretold by a progressive fall in the blood pressure over a period of weeks or months. A gradually falling blood pressure may also denote extreme atrophy of the kidneys with consequent under-production of renin. Indeed, in chronic nephritis a falling blood pressure is often a most unfavourable sign.

Uræmia.—Paradoxically, death from uncomplicated uræmia is not very common in chronic nephritis. Heart failure is by far the most common immediate cause of death. Some patients remain in the stage of compensated impairment of renal function for years, but once impairment of function occurs it does not improve.

Anœmia.—A hypochromic anæmia with low colour index is exceedingly common and may be very severe. As a rule the anæmia does not appear until renal function becomes impaired. It is roughly parallel to the degree of impairment, and may in turn cause further loss of function through insufficient oxygenation of the renal cells. If purpura occurs the platelet count is usually normal.

The Urine.—Albuminuria is almost constantly present in chronic glomerulo-nephritis. In the later stages albuminuria is less marked, and at times there may be only a trace or even none. Whereas diminution in the amount of albumin passed in the urine is generally a favourable sign in nephritis, the reverse is true when in chronic nephritis it marks the onset of severe contraction of the kidney and increasing impairment of renal function. Casts of many kinds, epithelial, fatty, granular, and hyaline, are also frequently present in the urine in early chronic nephritis. In the terminal stage they become fewer in number and may often be absent or represented by an occasional hyaline cast. Macroscopic hæmaturia is not a common feature of chronic nephritis except during acute exacerbations and when necrotising arteriolitis (malignant hypertension) supervenes. Red cells, however, are constantly found on microscopical examination throughout the course of the disease.

Diagnosis.—In children and adolescents in whom albuminuria may be the only abnormal feature, the diagnosis has to be made from the benign

albuminurias described above (*vide* p. 507). Hypertension with slight albuminuria may cause confusion with essential hypertension with commencing renal involvement. The differential diagnosis is often impossible, but it should be borne in mind that glomerulo-nephritis most often occurs under thirty years of age and essential hypertension over this age. Polycystic disease of the kidneys may simulate glomerulo-nephritis, but the kidneys are generally obviously enlarged and characteristic changes are found in the renal pelves with the aid of a pyelogram. The diagnosis from long-standing pyelo-nephritis is often completely impossible, though here, also, pyelograms may assist. Anæmia may be so profound as to suggest pernicious anæmia or leukæmia. It should be remembered in this connection, too, that uræmia is a frequent cause of " idiopathic " purpura in middle age and over. Myxœdema also may superficially resemble chronic nephritis.

Prognosis.—Chronic nephritis is ultimately fatal. Two factors govern the duration of this stage—cardiovascular complications and impairment of renal function. Life may continue for several years with both, but once symptoms arise from either, a fatal issue is to be expected, generally within a few months. In all patients and at all stages of the disease, intercurrent infections constitute a grave danger.

Treatment.—Treatment is essentially palliative, though much may sometimes be done to prolong life and make it more tolerable. The immediate object of treatment is to secure rest for (*a*) the kidneys and (*b*) the heart. This is achieved not only by physical rest in bed but by appropriate adjustments of the diet and fluid intake and the administration of drugs according to the clinical and biochemical state of the patient.

Regime.—Confinement to bed for an initial period is nearly always advisable. This should be continued, whether it be for a period of weeks or months, until it is considered that no single sign or symptom is likely to improve further. The process of getting the patient up must be effected slowly and, graded by the use of the couch, chair, and walking, successively. Elderly patients, however, suffering from marked renal insufficiency which is known to be of long duration and who have been ambulant, should not suddenly be confined to bed as they have often become attuned to their state and are unable to readjust themselves rapidly to new conditions.

Diet.—The diet in chronic nephritis should be regulated by the renal function. Renal function tests should therefore be performed at frequent intervals. So long as renal function remains normal and there is no macroscopic hæmaturia, a full allowance of protein may be given. There is no evidence that red meat is more harmful than so-called white meat, such as fish or chicken. The total quantity of protein need only be diminished when evidence of decompensation occurs, *i.e.*, when the blood urea increases. Even then it is generally possible and desirable to permit meat at least once a day. Under no circumstances must the protein intake be allowed to fall below 0·7 gm. per kilo of body weight *per diem*, except in emergencies, and then not for a longer period than ten to fourteen days. Prolonged protein deprivation leads to anæmia with further diminution of renal function and increased endogenous protein katabolism.

Salt Intake.—Restriction of salt should be imposed (*a*) when œdema is a prominent feature, (*b*) with cerebral or cardiac symptoms resulting from marked hypertension, and (*c*) with prolonged macroscopic hæmaturia. It is generally sufficient to omit added salt but to allow that used in cooking,

except in the treatment of hæmaturia and acute hypertensive encephalopathy, when an absolute salt-free diet is important.

Fluid Intake.—When impairment of renal function and œdema coexist the former must take precedence in treatment and the fluid intake should be increased to that which will produce the maximum volume of urine, even at the risk of increasing the œdema. If as a result of increasing the fluid intake the urinary volume is not augmented, then diuretics as indicated in the next paragraph must be employed in addition. When renal function is normal, as it usually is when œdema is a marked feature, the fluid intake should be restricted, but to not much less than the volume of urine for the preceding twenty-four hours, and never to the point of inducing thirst.

Drugs.—Digitalis may be used in myocardial failure, whether hypertension is present or not. As in acute nephritis, diuretics should not be used as a routine in the presence of macroscopic hæmaturia. They should be employed as an aid to inducing polyuria as mentioned above, and for this purpose potassium citrate by mouth is the most useful. It should first be ascertained that the potassium content of the blood is not already above normal. Mercurial diuretics, such as mersalyl, are contraindicated. Iron may be given as iron and ammonium citrate (90 to 120 gr. *per diem*) for anæmia, and occasionally blood transfusion is required in extreme emergencies, but the danger of subsequent anuria is very great even with careful grouping, and as a rule it is strongly contraindicated, especially in elderly subjects. For violent headaches which do not respond to low salt diet, hypertonic magnesium sulphate (5 per cent. solution) may be given rectally twice daily, or nitrites, bromides, barbiturates, or morphine may be given. Venesection followed by lumbar puncture is, however, often more effective. The fluid balance in the body, and particularly the volume of urine excreted, should never be upset by the giving of purges. Only liquid paraffin or simple enemata should be given. For similar reasons, diaphoresis is undesirable. Large quantities of fluids of any kind should never be given intravenously.

Surgical Treatment.—Infective foci, such as septic tonsils, sinuses, and teeth are generally better left untouched, but acute conditions such as mastoiditis or appendicitis must be dealt with surgically.

Sub-clinical Glomerulo-nephritis

This, the least spectacular variety of glomerulo-nephritis, is in one respect the most important, for although there are no symptoms and few signs, it is undoubtedly the cause of the great majority of cases of chronic glomerulo-nephritis in whom no history of a previous attack of acute nephritis is obtainable. The patient is always entirely unaware of its existence and the physician generally is, unless from being aware of the possibility or for some other reason special search is made. The introduction of a quantitative method of studying the formed elements in the urine (the Addis sediment count), more delicate tests of renal function, statistical inquiries into the correlations between glomerulo-nephritis and other diseases, and the critical examination of microscopical sections of kidneys from subjects without frank renal disease and dying from numerous other, mainly infective or post-infective diseases, show that low-grade glomerulo-nephritis without symptoms is an exceedingly common condition. Few kidneys, in fact,

on careful examination fail to show some evidence of previous healed glomerular damage. In the majority the lesions are slight and focal in distribution and the recovery rate must certainly be very high. Probably, too, in the majority the most careful laboratory investigations would fail to reveal any abnormalities. In some, however, and the total number must be very large, secondary or symptomatic nephritis of this kind and degree undoubtedly occurs in and after infections and fevers of many kinds. Its potential importance as a source of later chronic glomerulo-nephritis is so great that more thorough investigation in, and stricter criteria regarding recovery from, and return to work after, infections in general should be adopted. It is perhaps less important at present to determine whether this variety of glomerulo-nephritis is to be regarded as a form of focal nephritis, or as a latent stage of diffuse nephritis, than it is to recognise its prevalence and significance. It can only be diagnosed by repeated search for intermittent and slight albuminuria, or the occasional presence of a few red blood cells or casts, during or following an acute infection. When discovered it should, of course, be most thoroughly treated in spite of the apparently trivial signs. Treatment includes rest in bed, moderate alkalinisation of the urine, a normal diet, and return to full activity in stages regulated by the urinary signs, the alkali reserve of the blood and the blood sedimentation rate, as in the period of recovery from frank acute nephritis.

Focal (Non-embolic) Glomerulo-nephritis

This variety occurs mainly in children suffering from a number of acute infections, notably streptococcal tonsillitis and mastoiditis, and less frequently from pneumonia, scarlet fever, erysipelas, typhoid, measles, rheumatic fever, and some forms of purpura. In contrast with diffuse nephritis it is supposed to occur at the height of the primary infection instead of after an interval. Most authorities no longer accept this. Unlike the diffuse form, too, it is stated that the causal organism is sometimes found in the kidneys and in the urine. The essential lesion is an acute glomerulitis affecting only comparatively few glomeruli and only *individual loops* of a single tuft. Neither hypertension, azotæmia, nor œdema are therefore to be expected, and do not occur. Clinically the disease is characterised by sudden and often profuse hæmaturia which often clears in the course of a few days, though sometimes a few red cells persist in the urine for many months. Albuminuria is present but usually not in excess of the amount of blood. Casts of all kinds appear at the onset. The prognosis is almost invariably favourable except in rare instances in which repeated attacks ultimately involve a large proportion of the nephrons, and renal function becomes impaired. It is very doubtful whether this variety is a distinct form of acute nephritis and not merely a mild type of acute diffuse nephritis.

Focal Embolic Glomerulo-nephritis

(*Multiple Glomerular Embolisation*)

This variety of acute nephritis occurs only during the active (bacteriæmic) stage of subacute bacterial endocarditis, in which it causes repeated transient attacks of hæmaturia without œdema, hypertension, or azotæmia. Bacterial emboli are lodged in the glomerular tufts. It is quite distinct from the

non-embolic diffuse glomerulo-nephritis which so frequently complicates the later inactive (non-bacteriæmic) stages of subacute bacterial endocarditis and leads to progressive renal insufficiency and death from uræmia.

Acute Interstitial "Nephritis"

This comparatively rare condition gives no indication of its presence during life, and is really not a form of nephritis at all, in that the nephrons are not affected, although it is customary to describe it under this name. Microscopically the essential lesion is a focal infiltration of the interstitium of the kidney with lymphocytes. It does not give rise to symptoms. It occurs chiefly in children in the course of very severe and fatal streptococcal infections such as tonsillitis, scarlet fever, and septicæmia.

THE NEPHROSES

The word nephrosis was introduced by Mueller in 1905 to distinguish the primary degenerative from the primary inflammatory nephropathies. Nephrosis may be defined as *a primary non-inflammatory degeneration of the renal parenchyma* (*tubules*) and therefore includes a large variety of pathological changes and their clinical counterparts, ranging from a transient cloudy swelling of the cells of the tubules, as in febrile albuminuria, to the most extreme lipoid degeneration of these cells as in chronic lipoid nephrosis. Some authorities restrict the term "nephrosis" entirely to chronic cases, the chief pathological change in which is a lipoid infiltration of the tubular epithelium, but it would seem more logical to adopt the wider definition given above and to classify the main sub-varieties thus: (i) larval, (ii) necrotising, (iii) acute, and (iv) chronic—simple and lipoid nephroses.

Larval Nephrosis

This is characterised clinically by albuminuria and pathologically by cloudy swelling, and sometimes fatty degeneration of the tubular epithelium. Under this heading are included the febrile albuminurias and the albuminuria of pulmonary tuberculosis, jaundice, pernicious anæmia, and of many other conditions. Renal function is rarely impaired and œdema and hypertension do not occur. It must be differentiated from a low-grade sub-clinical nephritis (*vide* p. 530), but apart from this it has no clinical significance. Recovery is the rule and no treatment is required.

Necrotising Nephrosis

This is similar to the preceding variety in its pathology but the degenerative processes are more severe, and actual necrosis of the tubular epithelium is present, so that renal function may be grossly impaired. It occurs only occasionally after infections, and then generally in very severe cases. Necrotising nephrosis most commonly results from poisoning with various chemical agents, particularly with the salts of the heavy metals such as mercury, bismuth, and gold. It is most frequently encountered as a result of poisoning with bichloride of mercury. It may also result from poisoning

with phosphorus, neosalvarsan, chloroform, and lysol, and may complicate burns, yellow fever, cholera, diabetes, and high intestinal obstruction. It causes oliguria and anuria, which, unless relieved, lead to death from uræmia.

Acute Nephrosis

This is clinically a fairly distinct group, though pathologically it may only be an exaggerated example of the larval variety. It occurs mostly in young children, in whom marked generalised œdema with gross albuminuria arises, either without obvious cause or following an acute pneumococcal infection. The kidneys are large, smooth, soft, and pale or congested. Microscopically the chief lesion is a well-marked cloudy swelling of the renal tubules. Although the onset is comparatively rapid, the course may be slow and the condition may become chronic. It is believed that approximately a third of the cases recover after some months, but in others relapses are common, often caused by some intercurrent infection. Such episodes are often fatal. Pneumococcal peritonitis is a frequent complication, and accounts for many deaths, though it is not invariably fatal. Surgical intervention for pneumococcal peritonitis complicating any form of nephrosis is of uncertain value. The proportion of recoveries is about the same with or without open operation, and the writer is now inclined to avoid surgical interference, first giving penicillin and then, if necessary, removing purulent effusions by aspiration.

Chronic Nephrosis

There is probably no essential difference between simple chronic nephrosis and chronic lipoid nephrosis, the latter term being used to describe those cases in which lipoid changes are most marked. There is perhaps a tendency for these latter cases to run an even more chronic course.

Munk, in 1913, pointed out that chronic parenchymatous nephritis (large white kidney) really comprised two distinct diseases with a quite different origin, course, and termination. The vast majority began as an acute diffuse glomerulo-nephritis, though this phase was often inconspicuous, and terminated in azotæmia with hypertension. This group is now termed the nephrotic (subacute) stage of chronic glomerulo-nephritis. There is also a smaller group, indistinguishable from these clinically and biochemically, but in whom no history of an origin from acute glomerulo-nephritis could be obtained, and who rarely, if ever, developed either azotæmia or hypertension. This form of Bright's disease is now known as chronic nephrosis. It is a rare disease, and *the majority diagnosed as such on clinical grounds are later discovered to be examples of the nephrotic stage of glomerulo-nephritis.* However, numerous authenticated examples have now been described, and most authorities admit its claim as a distinct variety of Bright's disease. Pathologically the kidney is enlarged, soft, smooth, and pale, with a capsule which strips readily. The cut surface looks and feels greasy and contains numerous yellow areas of fatty degeneration. Microscopically the chief lesion is a marked degeneration with fatty change in the cells of the proximal convoluted tubules. There is a considerable deposition of doubly refractile lipoids in the cells. The lumen of the tubules is often filled with epithelial debris and casts. Regeneration of tubular cells is common. The glomeruli with ordinary stains appear normal, but with special staining methods

thickening of the basement membranes of the capillaries of the tuft and of Bowman's capsule is seen. These changes, though slight, are constantly present and are of great theoretical importance, as suggesting that chronic nephrosis should no longer be regarded as a degeneration confined to the tubules but that a glomerular element is also present, though whether this is of primary importance is not yet known. It is also believed by some that there is a late or terminal stage, in rare instances of chronic nephrosis, in which the kidney becomes contracted and granular.

Ætiology.—Chronic nephrosis is essentially a disease of childhood and young adult life. Sometimes the disease follows infections elsewhere in the body, such as syphilis, diphtheria, pneumonia, and tuberculosis, but in the majority it arises without known cause.

Pathogenesis.—The outstanding clinical feature of chronic nephrosis is the gross œdema and anasarca associated with marked albuminuria. The œdema is due mainly to diminution of the colloid osmotic pressure of the blood plasma from fall in the protein content, particularly the albumin fraction. Diminution of the plasma protein is due chiefly to loss of albumin in the urine. What causes the albuminuria is not known. Several theories are held as to the pathogenesis of chronic nephrosis. Many believe that chronic nephrosis begins as acute glomerulo-nephritis and that there is, in fact, no such condition as primary chronic nephrosis ; others consider that it is a primary degenerative disease of the kidney in which increased permeability of the renal filter is so great that molecules as large as those of albumin get through. Since albuminuria is believed to be glomerular in origin, the lesions described above in the glomeruli of chronic nephrosis have an added significance ; some accept Epstein's theory that chronic nephrosis is a primary metabolic dyscrasia and that the renal lesions are secondary.

The Clinical Picture of Chronic Nephrosis.—The onset is usually very insidious and there may be a preliminary period of weeks or months of vague ill-health and lassitude. The first symptom is often a mild swelling of the face or feet in ambulant patients, which gradually spreads to all parts of the body and increases in severity until the dropsy becomes extreme, involving the extremities and serous cavities. A characteristic of this disease is the manner in which the œdema waxes and wanes, without obvious cause, over periods of months or years. Accompanying the œdema is a high degree of albuminuria, and during the periods when œdema is forming or is increasing there is marked oliguria. Casts may be present in the urine, at times in enormous numbers. Epithelial and granular casts predominate and fatty casts may be found. Gross hæmaturia does not occur, though a few red cells may sometimes be found on microscopical examination. Hypertension is absent. There is no disturbance of renal function, and the specific gravity of the urine is usually high, even after correcting for the large amount of protein present. A characteristic feature of the blood chemistry is the diminution in the total protein content of the plasma and especially of the albumin fraction. Accompanying this there is often a marked lipæmia and hypercholesteræmia. The chloride content of the plasma is on the whole high and that of the œdema fluid higher still. The chloride content of the urine is correspondingly low, and indeed chlorides may be almost absent from the urine. The protein content of the œdema fluid is extremely low (generally less than 0·1 per cent.). It often has a milky or opalescent appear-

ance, due to the presence of lecithins. Doubly refractile lipoids are frequently present in the urine, but are not characteristic, and are often met with in other conditions, notably the nephrotic stage of chronic glomerulo-nephritis. The plasma volume is not increased except just prior to the onset of diuresis. Despite the pallor, anæmia is not a striking feature and severe anæmia is rare. Both water and chloride elimination are diminished, but the defect is chiefly or entirely extra-renal. Since renal function is normal, uræmia does not occur. The basal metabolism is often extremely low. Apart from retinal œdema no form of retinopathy occurs.

Sufferers from chronic nephrosis are specially susceptible to intercurrent infections, and these constitute the chief danger to life. Pneumococcal infections are the most common, and death from pneumococcal peritonitis is frequent, especially in children. In older subjects, streptococcal infections are relatively more common than in children. Erysipelas may occur, spread rapidly, and prove fatal.

It is doubtful whether chronic lipoid nephrosis differs from chronic simple nephrosis except in degree. The comparatively few well-authenticated cases described mainly indicate an even more chronic and severe form of the latter disease. All the signs and symptoms, but especially the lipoid changes in the blood, urine, and kidneys, are more pronounced, of longer duration, and are less subject to spontaneous remissions or amenable to treatment.

Diagnosis.—The chief difficulty in diagnosis is to differentiate chronic nephrosis from the nephrotic stage of chronic glomerulo-nephritis. This is sometimes possible when there is a definite history of an attack of acute nephritis, or gross hæmaturia following a sore throat or scarlet fever, but often the distinction cannot be made. The subsequent appearance of hypertension or azotæmia may, of course, determine the diagnosis. From amyloid nephrosis the diagnosis may again prove difficult or impossible. A history of long-continued bone sepsis or tuberculosis may help, and enlargement of the kidneys, liver, and spleen suggest a diagnosis of amyloid disease. When there is only moderate generalised œdema the clinical appearance may simulate myxœdema.

Prognosis.—The disease, if not cut short by intercurrent infections, normally runs a very prolonged course, with periods of months or years of remissions and exacerbations. Some patients, especially children, recover completely, but on the whole the prognosis is not good.

Syphilitic nephrosis is an important variety which occurs chiefly during the secondary stage of syphilis, and is characterised mainly by gross albuminuria with relatively few or no casts, and in Great Britain little or no œdema, though sometimes this may be extensive. Many patients respond well to antiluetic treatment, but exceptions occur in which non-specific treatment is more effective.

Treatment of Chronic Nephrosis and the Nephrotic Syndrome

Diet.—The main indications are for a diet high in protein but low in salt and fluid content. In only a minority does a high protein diet alone clear up œdema, and then only in the milder cases and especially in children. Often, too, it does not materially increase the protein content of the plasma. Protein to the extent of 120 to 200 gm. *per diem* may be given. Foods

which contain the maximum of protein and the minimum of salt should be used, such as eggs, steamed fish, meat, and National dried skimmed milk. When œdema is extreme and is causing urgent symptoms, it may be wise to rely at first on the vigorous use of diuretics because of their more rapid action, combined with a low protein diet. A high protein diet (when first used) retards the effect of most diuretics and should be omitted until the bulk of the œdema has been removed, when it should always be given. The course of chronic nephrosis is so prolonged that a strict salt-free diet cannot be maintained throughout. It should only be used in conjunction with diuretics and then that recommended for acute nephritis will be found suitable (*vide* p. 532). At other times the salt intake should be restricted to about half the normal, which may be achieved by forbidding added salt but permitting that ordinarily used in cooking. The fluid intake should be mildly restricted to the minimum which can be taken with comfort. There is great danger in too rigid a restriction of fluid, especially in children. Thirst should not be allowed. Generally, between two and three pints per twenty-four hours will suffice for adults.

Medicinal Treatment.—The value of diuretics in chronic nephrosis has been underestimated, chiefly through insufficient experience in their use. The custom of trying one diuretic after another in a more or less perfunctory manner is to be deprecated. It is as well to remember that many diuretics cause a temporary increase of oliguria and œdema before diuresis sets in, and that this is not necessarily an indication that they are doing harm and should be discontinued but rather that they should be employed for longer periods and used more vigorously.

Diuretics.—*Salts.*—The monovalent kations alone are absorbed from the alimentary tract with sufficient readiness for general use. Of these, potassium is the most powerful diuretic. Sodium should not be employed except as a brake on the action of potassium, and to counteract the toxic effects of the latter when used in very large doses. Potassium is generally given either as the citrate or chloride, and the former is more effective. Multivalent kations, such as calcium, are best given by intramuscular injection. Salts which produce acidosis, such as ammonium chloride and calcium chloride, may be employed. In practice their use is limited : firstly, because they cannot be given in effective doses for a sufficient length of time without causing severe gastro-intestinal disturbance ; and secondly, there is danger of increasing the existing acidosis of renal insufficiency when this is present, *i.e.*, in patients in the nephrotic stage of chronic glomerulo-nephritis.

Alkalis.—Potassium citrate, with the addition of a suitable proportion of sodium bicarbonate, is the most generally useful diuretic and the most certain in its action. It may be given for very long periods, even years, in effective doses without upsetting the gastro-intestinal tract, so that it is of value not only for the reduction of œdema but for preventing its recurrence. Additional advantages are that a high protein diet may be given at the same time, whilst if renal function is normal it is non-toxic. When renal function is impaired the danger of alkalosis arises, and potassium citrate in large doses should not be given unless facilities for immediate blood analyses are at hand. Very large doses may be required, up to 1,000 gr. or more per twenty-four hours. The amount given must be varied from time to time to suit changing conditions.

Urea is a safe and simple diuretic in doses of 15 gm. by mouth, thrice

daily. It is uncertain in its action, has to be continued for long periods, confers no protection against recurrence, and is effective in comparatively few cases.

Purine Derivatives.—Caffeine, theobromine (as theobromine sodium salicylate or diuretin, 10 to 20 gr.), and theophylline or theocin (2 to 4 gr.) are occasionally of value in cases of renal disease in which the dropsy is mainly due to cardiac failure.

Mercurial Diuretics.—Mersalyl and Neptal are of the greatest value in dropsy due to cardiac failure, and are sometimes of use as adjuncts in the treatment of nephrosis with alkalis. Impairment of renal function, however, is an absolute contraindication to their use. Sudden death occasionally follows their intravenous administration even when renal function is normal. Full details as to their administration are given elsewhere (*vide* p. 418).

Bismuth Salts.—Bismuth sodium tartrate, injected intramuscularly in doses of 0·03 gm., is also a powerful diuretic, but again is contraindicated with impaired renal function.

Thyroid Extract.—Thyroid may be given in increasing doses up to 15 gr. of the dry extract daily, and even larger doses are sometimes required. It is rarely successful when used alone, but is said to be occasionally a valuable adjuvant to other methods of treatment.

Parenteral Colloid Administration.—In addition to a high protein diet various methods have been tried of increasing the colloid osmotic pressure of the blood plasma directly. Transfusions of blood and intravenous injections of gum acacia (1 gm. per kilo of body-weight in a 30 per cent. solution diluted with an equal volume of distilled water, and repeated every third or fourth day) may produce a copious though transitory diuresis. Blood transfusions may, however, induce a fatal anuria and should only be used in special circumstances. Daily intravenous injections of one or two pints of double or quadruple strength plasma solution, for about twenty days, causes a marked but temporary diuresis in some patients.

Diaphoresis and Purgation.—Both divert fluid from the kidneys and cause functional azotæmia. They are also exhausting to the patient and should never be employed.

Decapsulation.—The number of unequivocal examples of success resulting from this operation is very small, whilst the numerous failures are rarely reported. The operation is now rightly falling into disuse.

Mechanical Drainage.—Drainage of œdema fluid by paracentesis or Southey's tubes should not be undertaken except for the immediate relief of urgent symptoms due to pressure, or when other measures have failed. There are two dangers to be apprehended as a result of this procedure: first and most important, it leads to deviation of fluids from the kidneys and causes functional azotæmia, which is not uncommonly fatal; and secondly, there is a definite risk of local sepsis and erysipelas leading to fatal consequences. The strictest aseptic precautions must therefore always be observed. The site of puncture is of little consequence provided maximum drainage be secured. Fluid should be aspirated from the pleural cavities if the heart be displaced or embarrassed. If ascites is causing distress the fluid should be withdrawn. If there is possibility of a purulent effusion an exploratory aspiration may be required. In many cases mechanical drainage alone fails and is followed by a return of the œdema. Sometimes, however, diuretics of all kinds fail, and repeated drainage may be the only method

available and sometimes, though rarely, proves permanently successful in eradicating the œdema.

Removal of Foci of Sepsis.—There is no evidence that operations such as tonsillectomy or drainage of para-nasal sinuses are of value in chronic nephrosis. The rule should be to avoid interference in these cases unless the treatment of the local lesion itself is imperative.

Amyloid Disease of the Kidney

Amyloid disease of the kidney is sometimes classified with the nephroses because of its clinical resemblance to the latter. The essential lesion, however, is a primary degeneration of the renal vasculature—the glomerular vessels—the signs and symptoms (except in the rare cases of amyloid contracted kidney) are exclusively those of a nephrosis, namely, albuminuria and œdema without hypertension or azotæmia. Amyloid nephrosis is only found in association with long-standing suppuration, especially in chronic tuberculous lesions which become secondarily infected, pulmonary cavities and bone and joint disease, chronic empyema, osteomyelitis, bronchiectasis, and pyonephrosis. It may be met with in syphilitic bone disease with infected sinuses. Amyloid change is generally present in other organs as well, notably the liver and spleen. Clinically the chief features are gross albuminuria leading to generalised œdema. In rare instances a secondary contraction of the kidney develops with impairment of renal function, loss of œdema, and even hypertension. The diagnosis is often difficult or impossible, on account of the clinical similarity to chronic nephrosis. The presence or history of long-continued sepsis or tuberculosis, enlargement of the kidneys, liver, or spleen may be of value. If 10 to 15 c.c. of a 0·75 to 1·2 per cent. solution of Congo red be injected intravenously, 30 per cent. of it disappears from the blood in normal persons in one hour, but in amyloid diseases and chronic nephrosis 60 per cent. or more is removed. In amyloid disease, however, practically none of the dye appears in the urine, whereas in nephrosis most of it does. Amyloid disease is usually fatal. Instances of complete recovery, however, have been recorded. The treatment is essentially that of the underlying condition and the administration of a high protein diet which may be supplemented with increasing doses of thyroid extract. Diuretics may be tried, but are usually less successful than in chronic nephrosis.

PREGNANCY AND RENAL DISEASE

The renal complications and sequelæ of the pregnancy toxæmias (pre-eclampsia and eclampsia) are important because of their prevalence and high mortality.

Symptoms.—Briefly the chief symptoms are albuminuria, œdema, and hypertension, any of which may precede the others by days or weeks. Often all appear simultaneously and suddenly. Accompanying these cardinal features there may be oliguria, headaches, retinal hæmorrhages, white patches of hypertensive retinopathy, amaurosis, and sometimes detachment of the retina. Hæmaturia and nitrogen retention do not occur except occasionally in the later stages of very severe attacks. If improvement

does not occur the symptoms increase and are followed by convulsions and coma—the hall-marks of eclampsia. It will be observed that many of the symptoms are those of increased intracranial tension.

Morbid Anatomy.—Some maintain that the often inconspicuous changes in the kidneys are not specific but represent abortive and mixed lesions of glomerulo-nephritis and nephrosis. Others describe typical lesions amongst which are hyaline droplet and fatty degeneration of the cells of the convoluted tubules and the epithelium of the glomerular tuft, and fairly constant thickening of the basement membranes of the tufts. Arterial changes are insignificant. The lesions are primarily degenerative and the condition has been called glomerulo-nephrosis.

Sequelæ.—These must be considered under two headings: (1) those initiated by pregnancy, and (2) pre-existing renal disease complicated by pregnancy.

1. The form of Bright's disease which most commonly arises from pregnancy toxæmia is a permanent and progressive hypertension identical clinically and pathologically with the essential hypertension and nephrosclerosis of the non-pregnant. It occurs in from 25 to 50 per cent. of patients surviving the acute stages of pregnancy toxæmia. It is more likely to follow recurrent toxæmia than a single attack, and the duration of the toxæmia is a more potent causal factor than its intensity. Persistent hypertension, therefore, more often follows pre-eclampsia than eclampsia.

2. Of pre-existing forms of Bright's disease, pregnancy is most likely to be met with in (*a*) subacute or chronic glomerulo-nephritis and (*b*) essential hypertension: (i) An existing glomerulo-nephritis is generally but not invariably made worse by pregnancy; also, it greatly increases the chances of the pregnancy being complicated by toxæmia. Pregnancy, therefore, should not be allowed to occur or to continue in glomerulo-nephritis. (ii) When pregnancy supervenes in pre-existing essential hypertension, the latter is unaffected in about half the cases. Pre-existing hypertension, however, increases the liability to pregnancy toxæmia about five times. Pregnancy toxæmia causes a permanent increase in the hypertension of a pre-existing hypertension in about 25 per cent. of the cases. Pregnancy, therefore, should be avoided in essential hypertension.

Treatment.—It is obviously important (*a*) to prevent toxæmia if possible, and if not (*b*) to shorten its duration. Preventive treatment is either medical or surgical. By far the most effective is adequate antenatal supervision, which may with advantage be supplemented by prophylactic alkalinisation, as described in scarlatinal nephritis (*vide* p. 522). This diminishes the incidence of recurrent toxæmia by about 25 per cent. if begun at the onset of pregnancy and continued throughout. If albuminuria or other signs of toxæmia develop in spite of these measures, then strict confinement to bed and a low-salt diet should be prescribed as well. The majority clear up with this treatment, but if after three weeks there is not sufficient improvement, induction of labour must be seriously considered. The medical treatment of the severer grades of toxæmia is essentially that of nephrosis with gross œdema and hypertensive encephalopathy—alkalinisation with potassium citrate (sodium salts alone are contraindicated), low-salt diet, and limited fluid intake; venesection followed by lumbar puncture, intravenous hypertonic solutions of salt (30 c.c. of a 30 per cent. solution) or sucrose (100 c.c. of a 50 per cent. solution), and the free use of narcotics such as chloral, the

barbiturates, and morphia, but preferably not chloroform. Purgation and diaphoresis are contraindicated.

Bilateral Cortical Necrosis of the Kidneys.—This is a comparatively rare condition consisting of extensive infarction and necrosis of the renal cortex, believed to be due to spasm and thrombosis of the cortical vasculature (*vide* p. 517). It is characterised by anuria, azotæmia, and renal insufficiency, and sometimes by hæmaturia and hypertension. It is mainly (75 per cent.) associated with pregnancy and pregnancy toxæmia. Recovery is possible, though rare. Treatment is as for anuria (*vide* p. 516).

THE PRIMARY NEPHROSCLEROSES

The third and largest group of disorders included in the term Bright's disease is that comprising the Primary Nephroscleroses. It consists of three sub-groups :—

Renal—

1. Arteriolosclerosis (known clinically as essential (benign) hypertension).
2. (Necrotising) arteriolitis (known clinically as malignant hypertension).
3. Arteriosclerosis (which has no clinical significance).

Whilst malignant hypertension may apparently arise *sui generis*, it often occurs as a terminal complication or phase in other varieties of renal sclerosis, viz., chronic glomerulo-nephritis, chronic pyelonephritis, and pituitary basophilism.

Renal arteriolosclerosis and renal arteriolitis together constitute the pathological basis of the large group of disorders often referred to as cardio-vascular renal disease, which is directly and indirectly the most common cause of death in Great Britain and many other countries. Renal arteriolosclerosis is, of course, vastly more important numerically than renal arteriolitis. General, as distinct from renal, arteriolosclerosis and arteriosclerosis are described elsewhere (*vide* p. 426).

Renal Arteriolosclerosis

(*Syn. : Kidney of Essential Hypertension ; Primary Granular or Red or Small Red Kidney ; Chronic Interstitial Nephritis (major part of)*)

In all cases of essential hypertension the renal vasculature is to some extent involved, but only in about 10 per cent. are the renal lesions sufficiently pronounced to cause death from renal failure. Essential hypertension is mainly a disorder of middle and late middle life, the maximum incidence being between forty-five and sixty-five years. It is equally common in both sexes.

Ætiology.—Renal arteriolosclerosis is a result of long-continued hypertension, itself probably due to unknown factors which cause a diminution of renal blood flow and liberation of renin into the circulation. Contributory factors are heredity, obesity, and the stress and strain of life under modern conditions. Lead, gout, and alcohol, formerly considered potent causes,

are probably now of little importance. There is no evidence that over-indulgence in food (protein) or tobacco is of ætiological significance.

Morbid Anatomy.—The kidneys vary in size and appearance from normal to being small, red, and granular. The capsule is adherent and the surface finely granular. There is an excess of fat in the pelvic region. On section the organ is hard and tough, and the cortex is narrow and not well differentiated from the medulla. Small cysts may occur beneath the capsule. Histologically the earliest lesion is a thickening of the intima of the afferent arterioles and their parent vessels with fatty degeneration and occlusion of the lumen. The corresponding glomeruli undergo hyaline and fatty changes, fibrosis, and atrophy. The tubules atrophy and are replaced by fibrous tissue. At first these changes are confined to small localised areas separated by larger areas of normal kidney. Later the whole kidney becomes replaced by fibrous tissue and few normal elements remain. Even in this stage death occurs in the majority from heart failure and cerebral hæmorrhage. The remainder die from renal failure and uræmia. Death from uræmia may also occur when renal arteriolosclerosis has not advanced to this extent but when it has become complicated by renal arteriolitis or malignant hypertension.

Symptomatology.—The symptomatology of renal arteriolosclerosis (primary granular kidney) is, in the early stages which may be of many years' duration, that of essential hypertension, which is discussed elsewhere (*vide* p. 429). The only signs and symptoms which can be attributed directly to the renal involvement are (*a*) changes in the urine, such as mild albuminuria and the presence of an increasing number of casts, and (*b*) the usual signs and symptoms of impairment of renal function and of renal insufficiency which have been fully described above (*vide* Uræmia, p. 512). Compensatory polyuria, generally evident as nocturia and one of the earliest and most constant signs, is really evidence of impaired renal function. Albuminuria is usually slight and may be intermittent. Large quantities generally mean either that cardiac failure or the malignant phase has supervened. Hyaline and occasionally granular casts are often present, and again in the malignant stage may be abundant. Red blood cells are not found in the "benign" phase.

Renal Arteriolitis.—This condition is known clinically as malignant hypertension (*vide* p. 430) because in contrast to essential hypertension it tends to run a rapid and inevitably fatal course, often of only a few months. It is also apt to occur in the comparatively young, the age incidence in general being some ten years lower than in the essential type.

The kidneys are of normal size, slightly granular, of reddish colour mottled with yellowish areas and hæmorrhages. Microscopically the essential lesion is a necrosis and endarteritis of the afferent and interlobular arterioles. As already indicated, these changes are frequently found in association with those of other causes of renal sclerosis. Experimental evidence suggests that renal arteriolitis is essentially a more intense form of renal arteriolosclerosis, differing from the latter in degree rather than in kind.

The main clinical features of malignant hypertension (*vide* p. 430) are those of increased intracranial tension—headache, vomiting, amaurosis, papillœdema, convulsions, coma, and other manifestations of hypertensive encephalopathy. Renal function is grossly impaired, as shown by renal

function tests and fixity of the urinary specific gravity at 1010 (*vide* p. 431). Death occurs from uræmia and cardiac failure. Albuminuria is marked, red cells are constantly present in the urine, and attacks of gross hæmaturia frequently occur. Hyaline and granular casts are numerous. Clinically, malignant hypertension presents itself in two forms : either the patient, who is often relatively young, is unaware of previous hypertension, and attends for the sudden onset of violent headaches, " bilious attacks," or amaurosis ; or perhaps retinal changes are found on routine examination, or similar symptoms develop, more or less gradually, in one long known to be the subject of hypertension. The course in the former group is generally more rapid.

Renal Arteriosclerosis

This differs from arteriolosclerosis in affecting the medium size vessels only. It is primarily a disease not of the intima but of the media, is not accompanied by hypertension, unless, as often happens, essential hypertension also is present, and it is chiefly a disorder of old age. The kidneys are not seriously affected and never sufficiently to give rise to symptoms. Renal arteriosclerosis is not therefore a clinical entity.

Lead Nephritis in Children.—Nye has described a form of chronic nephritis in children which is prevalent in Queensland. Clinically it is characterised by persistent hypertension with cardiac hypertrophy, hypertensive retinopathy, chronic anæmia, and symptoms of uræmia. It appears that lead paint, used on the wooden veranda railings of houses, becomes blistered and powdery in the sun, and that the children get lead poisoning by licking the paint off the railings and their fingers. Statistical inquiry showed that nearly all the victims were habitual nail-biters. Histologically the lesions principally affected the renal vasculature. The course is one of progressive destruction of renal tissue and death from uræmia.

Renal Dwarfism (Syn. : Renal Infantilism, Renal Rickets).—Renal dwarfism is defined by Barber as " a condition of stunted development, associated with bone deformities of the late rickets type, due to an insidious chronic interstitial nephritis of obscure ætiology." The sexes are about equally affected, and it may occur occasionally in more than one member of a family. The onset is insidious, and it may not be observed until six or seven years of age that development is retarded. In other cases evidence of renal insufficiency may be the first manifestation. Genu valgum is usually the most marked bony lesion, but the deformities may be widespread. Intelligence is unimpaired. The initial lesion appears to be a chronic progressive and possibly congenital nephritis. Histologically the renal lesions are of great variety and complexity. In some, typical arteriolosclerotic lesions are present, and in such cases hypertension, cardiac hypertrophy, and even retinal changes may be found. In others there are various forms of glomerulitis without marked primary vascular lesions or hypertension ; cardiovascular changes are in fact more often absent than not. Long-standing impairment of renal function induces increased excretion and diminished absorption of calcium. In the attempt to maintain the concentration of calcium in the blood at a normal level this substance is withdrawn from the soft growing bones with the production of the characteristic bony deformities. The prognosis is inevitably hopeless. Death from uræmia is the rule, often precipitated by intercurrent infection or injudicious

operative interference. Most cases die at or before puberty, but a few have been reported as surviving to the second or third decade. The treatment is that of chronic nephritis. Deformities may be controlled by mechanical means, but operations under general anæsthesia are to be avoided. Ultra-violet radiation aggravates the bony lesions and is contraindicated.

Renal dwarfism is sometimes associated with congenital hydronephrosis, chronic pyelonephritis, congenital cystic disease of the kidneys, and multiple renal calculi.

HYDRONEPHROSIS AND PYONEPHROSIS

Hydronephrosis is an aseptic retention of urine in the kidney or renal pelvis due to obstruction to the flow of urine. It may be unilateral or bilateral, congenital, or acquired.

Ætiology.—Congenital hydronephrosis is rare and occurs usually in male infants as a result of congenital stenoses and septa in the ureter or urethra. It may accompany abnormal developments such as horse-shoe kidney or double ureters, or extra-renal anomalies such as spina bifida and imperforate anus. Acquired hydronephrosis may be due to (*a*) supra-vesical causes : calculi within the renal pelvis or ureters, torsions, thickenings and kinks at the uretero-pelvic junction, inflammatory septa and bands from chronic pyelitis, traumatic strictures following calculi, growths in the ureter and bladder, and compression of the ureter by abdominal tumours, movable kidney, aberrant vessels, abdominal adhesions and bands, chronic pelvic cellulitis, and malignant growths of the cervix uteri. (*b*) Infra-vesical causes : stones or foreign bodies in the urethra, strictures of the urethra and prostatic enlargement, pelvic tumours, enlargement of uterus, fibroids, ovarian cysts and growths, and uterine prolapse. Numerically the most important of these are impacted calculi, undue mobility of the kidney, and aberrant vessels. In not a few cases, however, no obvious cause can be found.

Pathology.—Whatever the cause, unrelieved obstruction, partial or intermittent, leads to dilatation of the ureter, pelvis, and calyces, and finally atrophy of the pyramids and cortex of the kidney. Ultimately the kidney is completely destroyed and replaced by a sac lined by fibrous tissue. A unilateral hydronephrosis does not cause renal insufficiency, owing to the hypertrophy of the unaffected kidney. A relatively small infra-vesical lesion will cause impairment of renal function as both kidneys become involved. In the latter, however, symptoms will develop more slowly, as the bladder acts as a reservoir which prevents serious back-pressure for a considerable time. Distended vessels on the inner surface of the hydronephrotic sac may rupture and cause hæmaturia.

Symptoms and Diagnosis.—In the early stages there may be no symptoms. Unilateral hydronephrosis is more liable to give rise to symptoms than the bilateral variety : pain usually occurs intermittently and simulates renal colic. There may be a continuous dull ache in the loin, vomiting, polyuria, and occasionally hæmaturia. In the later stages a tumour may be felt and the patient may be aware of its intermittent appearance.

Pyelography.—The study of renal disease, particularly hydronephrosis, tuberculous disease, and growths of the kidney, has been greatly facilitated by pyelography. Two methods are available : (i) Intravenous or excretion

pyelography ; in this a radio-opaque substance containing iodine is injected intravenously ; this renders the pelves of the kidneys and urinary passages visible by X-rays. (ii) Retrograde pyelography ; in this method sodium iodide is injected by ureteric catheter.

By one or both of these methods it is possible to detect early changes in the size or shape of the renal pelvis. In early hydronephrosis characteristic flattening or " clubbing " of the calyces can be readily detected.

Numerous proprietary drugs for intravenous pyelography are available, such as Pyelectan (Glaxo), Uropac (May & Baker), Uroselectan B (Schering), and Per-Abrodil (Bayer). The failure of a kidney to secrete the drug indicates impairment of function (*vide* p. 504). The only contraindications to the use of these drugs are severe kidney (azotæmia) and liver disease, and very acute inflammatory lesions of the urinary tract.

Prognosis.—The prognosis varies with the cause and the completeness with which it can be removed. The chief danger, apart from gradual destruction of the kidneys, is that the sac may become infected and result in a pyonephrosis.

Treatment.—The treatment is entirely surgical.

Pyonephrosis.—Pyonephrosis is a distension of the renal pelvis with pus. It arises as a sequel of pyelitis or from infection of a hydronephrosis. Renal calculi are the commonest cause. Tuberculous pyonephrosis is a not uncommon complication of tuberculous kidney (*vide* p. 105). The symptoms in the early stages of pyonephrosis are those of hydronephrosis, and the onset of infection is ushered in by pyrexia and rigors. The treatment consists of nephrectomy provided the function of the other kidney permits. The treatment of bilateral cases is purely palliative.

BACILLUS COLI INFECTIONS

Bacillus coli communis (B.C.C.) may appear in the urine without causing constitutional symptoms, a condition known as bacilluria. When coli bacilluria is accompanied by pyuria, inflammation of some part of the urinary tract has occurred. If the inflammation is confined to the renal pelvis the condition is known as *pyelitis* and if to the bladder *cystitis.*

Acute B.C.C. Pyelitis.—*B. coli* are the infecting organisms in the great majority of cases of acute pyelitis, the remainder usually being due to streptococcal and staphylococcal infections. In the majority the path of infection is believed to be by the blood stream but in some it is apparently an ascending infection from the bladder, either directly or through the peri-ureteral lymphatics. Whatever the path of infection, its location in the renal pelvis is determined by certain factors of which local trauma, either from external injury or internal injury from a calculus, obstruction to the urinary flow, and lowered resistance of the patient to infection in general are the most important. The presence of congenital abnormalities of the urinary tract, such as double ureters, horse-shoe kidney, or congenital stricture predispose to *B. coli* infections.

Pathology.—The local lesion consists of an acute inflammation of the mucosa and submucosa of the renal pelvis, which in chronic cases leads to ulceration and scarring, with consequent deformities.

Symptoms.—The symptoms of acute pyelitis are those of an acute

bacteriæmia, together with those of inflammation of some part of the urinary tract accompanied by bacilluria or pyuria. There may be a short prodromal stage with malaise, headache, anorexia, constipation, and perhaps frequency of micturition. In this stage the urine may contain only traces of albumin and a few leucocytes, and growth of B.C.C. is scanty. It is important to note that in the first few days it may not be possible to establish the diagnosis from examinations of the urine. The onset of the acute stage is sudden with great frequency, half- or quarter-hourly, strangury, abdominal pain, tenderness, and pseudo-rigidity. The temperature rises to 103° or 104° and there may be rigors. In some cases there is frank hæmaturia. Generally the urine is scanty, highly coloured with a very acid reaction, turbid or opalescent, and has a characteristic " fishy " odour. Constipation is present and there may be frequent vomiting. Later the pain becomes localised to one loin and is often of a dull, aching character. Headache may be a prominent symptom and toxic delirium and even coma may occur. The patient is flushed and the tongue is dry and coated. The affected kidney may be enlarged and tender. Leucocytosis is marked during the stage in which there is not much pus in the urine. When pyuria becomes abundant it decreases. Blood cultures are frequently positive in the earlier stages. In some the symptoms are chiefly those of cystitis, although the bladder may have been secondarily infected from the renal pelvis. With cystitis there is usually much mucus in the urine.

Course.—The course is very variable. The acute stage may subside in a few days or weeks. The temperature falls by lysis and the local symptoms disappear. In most cases bacilluria and pyuria persist in microscopical amounts for months after the actual symptoms have subsided. Recurrences are not uncommon after complete recovery and are usually precipitated by intercurrent infections, such as catarrhal colds or influenza, or by injudicious purgation. In severe cases the infection may spread and involve the renal parenchyma, a condition known as pyelonephritis or surgical kidney. Pyelitis in children occurs most commonly under two years of age, and almost exclusively in females. The constitutional symptoms are frequently very marked and out of proportion to the urinary signs. The disorder may begin as a gastro-intestinal disturbance or may closely simulate appendicitis or meningitis. It is one of the rare causes of rigors in children under two years of age, a fact which may be of some diagnostic importance.

Differential Diagnosis.—In the early stages with minimal urinary signs the malaise and pyrexia may simulate influenza, and the persistent headache typhoid. When the abdominal signs are marked, differentiation from an acute abdomen, *i.e.*, appendicitis, peritonitis, cholecystitis, or salpingitis may be difficult. A careful and repeated examination of the urine will generally lead to a correct diagnosis, though this may not be possible for a few days.

Chronic Pyelitis

Chronic B.C.C. Pyelitis is usually a residual infection of the renal pelvis, following an acute attack, and may persist for months or years or may be permanent. It may be quiescent or responsible for repeated acute attacks of pyelitis or cystitis. Sometimes the symptoms of pelvic infection are absent, though this is the cause of a persistent cystitis. The symptoms may

be general or local. Of the general symptoms, undue fatigue, headache, pain in the back, digestive disturbances, and symptoms of neurasthenia are the most common. The chief local symptoms are frequency of micturition, or urgency, and pain in the loin or region of the bladder. It is important to remember that bacilluria may persist indefinitely without symptoms of any kind and may be quite innocuous. Constipation is a predisposing cause of acute exacerbations of pyelitis in those with chronic bacilluria, but more frequently they are caused by the injudicious use of purgatives. Chronic pyelitis may give rise to pyonephrosis.

Treatment.—The first essential is to ensure that the pyelitis is a primary disorder and not a complication of some underlying condition such as a calculus. Strict confinement to bed is imperative in the early stages. The diet can be left to the wishes of the patient. Large quantities of fluids (not less than 6 pints per twenty-four hours), such as water, barley water, Contrexeville, or milk should be given. Purges should never be employed, as loose stools are contraindicated. The bowels may be kept open by paraffin or simple enemata.

The chief object of treatment is to maintain a large output of alkaline urine. Pus and organisms are literally washed out with the diuresis and the growth of the latter is inhibited by the alkalinity of the urine. Alkalis must therefore be given by mouth in doses large enough to render the early morning specimens of urine (the most acid of the twenty-four hours) persistently and definitely alkaline (pH = above 7·6) until all signs of inflammation have cleared, *i.e.*, usually for at least several weeks. As a rule the pyrexia, pain, and tenderness subside within forty-eight hours of the urine becoming definitely alkaline, but return at once if the degree of alkalinity be allowed to diminish. The beneficial results of alkali therapy, when adequate doses are given, are so consistent and striking that other treatment is rarely called for, and indeed failure to respond generally means either that the original diagnosis was wrong or that the condition is associated with mechanical obstruction in the urinary passages. In such cases further investigation by means of cystoscopy and ureteric catheterisation should not be delayed. Alkalis should be given as a mixture of equal parts of potassium citrate and sodium bicarbonate, 30 to 60 gr. of each, as many times a day as is found to be necessary to obtain and to maintain the required degree of alkalinity of the urine. The latter can be readily estimated daily (if necessary by the patient) in a very few moments, by noting the colour of a freshly passed specimen of urine after the addition of a few drops of a 0·1 per cent. solution of brom-thymol-blue, and comparing this with a standard indicator.[1] As a rule some 400 to 600 gr. of alkali per twenty-four hours will suffice, but even larger doses may be required, especially at the outset. As renal function is unaffected, no danger from alkalosis need be apprehended. Tincture of hyoscyamus (30 to 60 minims) may be added to the mixture as an antispasmodic if required. Alkali treatment must not be relaxed until by trial it is shown that a reduction of dosage is not followed by a return of pus or bacilli in the urine or of constitutional symptoms. In some cases it is necessary to continue treatment for months or years to prevent relapses. Alkalis will not, of course, be successful if mechanical obstruction to the flow of urine be present, as in the later stages of pregnancy.

[1] The "B.D.H." Capillator, supplied by the British Drug Houses Ltd., is a convenient form of apparatus for the purpose.

In such circumstances, and when it is not possible or desirable to deal immediately with the obstruction, other methods are indicated.

It has been found that growth of B.C.C. in the urinary tract may be readily and often completely inhibited when the urine is rendered sufficiently acid, especially in the presence of certain of the ketone bodies. For this reason the ketogenic diet was introduced for the treatment of B.C.C. pyelitis. As, however, the effective degree of acidity is very high it was necessary to supplement the diet, which was itself extremely unpleasant, by a rigid curtailment of the fluid intake in order to induce a sufficient concentration of " acid " in the urine. These conditions could often only be maintained sufficiently long to produce a temporary cure, so that the relapse rate was high. Pleasanter and much more effective is mandelic acid (Rosenheim), a substance related to the active principle (B-hydroxybutyric acid) of the ketogenic diet. Mandelic acid is given by mouth in doses of 3 gm. four times daily with ammonium chloride (15 gr.) to provide the optimum urinary acidity (*p*H 5·3). They are sometimes combined and given as ammonium mandelate (3 gm. three or four times daily). The fluid intake is restricted to less than 2 pints per twenty-four hours. Very encouraging results have been obtained but, chiefly because the treatment cannot be continued for sufficiently long periods without causing severe gastro-intestinal disturbances or damaging the kidneys, the relapse rate is high.

Sulphanilamide and sulphathiazole have been found to give the most remarkable results in B.C.C. infections of the renal pelvis, whilst sulphathiazole is particularly effective in infections of the urinary tract with staphylococci and streptococcus fæcalis. The dosage in adults should usually be a total of 3 to 5 gm. *per diem* and the course should last at least seven days. No dietary or fluid restrictions need be imposed as it is effective within a wide range of urinary reactions (*p*H 5·2 to 6·8). The sulphonamides are even more effective when given in conjunction with alkalis. They are particularly valuable in children and during pregnancy. In chronic pyelitis, after a thorough search has been made for mechanical causes of chronicity, such as impacted calculi and anatomical deformities due to scarring of the calyces and pelvis, sulphonamides should always be tried first and, if they fail, mandelic acid. Various so-called urinary antiseptics, hexamine, hexyl resorcinol, and numerous other substances are frequently employed, but the results are usually disappointing. Autogenous vaccines have long been in vogue but their value has certainly not yet been established. It must be admitted that the treatment of chronic B.C.C. pyelitis is often unsuccessful. The organism is, unfortunately, resistant to penicillin.

PERINEPHRIC ABSCESS

Perinephric abscess is a condition due to the formation of an abscess in the perinephric tissues, either as a result of a hæmatogenous infection from a distant focus, or more rarely by direct infection from the kidney or neighbouring structures. The infecting organism is nearly always the *Staphylococcus pyogenes aureus*.

Ætiology.—Perinephric abscess may result from direct injury to the loin or from staphylococcal skin infections—carbuncle, furuncle, or sycosis. The interval between the primary infection and the perinephric suppuration

is usually from two to four weeks, but may be as many months. It is occasionally due to streptococcal or pneumococcal infections and may follow tonsillitis, acute infectious diseases, and influenza.

Pathology.—The initial lesion is believed to be in the cortex of the kidney, in the form of minute abscesses which penetrate the renal capsule and so reach the perinephric tissues. Pus accumulates behind the kidney and may point in the loin, or it may travel down the psoas muscle to the groin or pelvis ; it may rupture through the diaphragm, enter the peritoneal cavity or the intestines, or by lymphatic spread infect the pleural cavities and cause empyema.

Symptoms.—The onset is usually insidious, with vague symptoms of fatigue, malaise, and pyrexia. Localising signs in the form of lumbago, pains in the loins or back, hip, or thigh may not appear for two, three, or many weeks. A limp may be the first obvious sign. Tenderness in and bulging of the posterior renal angle are important signs. There may also be thickening and induration of the skin in the loin. As the condition progresses, signs of toxæmia develop ; pallor, sweatings, high "septic" temperatures with or without rigors occur, and the leucocyte count increases to 20,000 to 40,000 per cubic millimetre. There may be diminution of the breath sounds and dullness on percussion over the base of the lung on the affected side. The diagnosis is confirmed by an exploratory puncture into the tumour. The urine is usually normal but may contain a trace of albumin and a few leucocytes. Some cases of what appears to be perinephric suppuration undergo spontaneous resolution.

Diagnosis.—In the early stages, lumbago, hip-joint disease, rheumatism, and sciatica may all be simulated. In the pyrexial stage the diagnosis from influenza, typhoid, septicæmia, tuberculosis, and infective endocarditis may be difficult.

Treatment.—If perinephric abscess is suspected large doses of penicillin should be given. Evacuation of the pus may later be necessary, but this should not be done until the suppuration is "ripe." If the temperature and suppuration continue after operation a renal carbuncle should be suspected. The prognosis is good in the vast majority of cases adequately treated.

Renal Carbuncle.—This is a circumscribed abscess of the cortex of the kidney, consisting of a fusion of a number of smaller abscesses separated by a zone of granulation tissue from the rest of the kidney. It is usually unilateral and is due to a hæmatogenous infection by the *Staphylococcus pyogenes aureus.* Ætiologically it is similar to perinephric abscess and usually follows furunculosis. The clinical signs are those of perinephric abscess and the diagnosis cannot usually be made before operation.

NEW GROWTHS

New growths of the kidney may be classified as :—

(*a*) Innocent tumours : lipomata, fibromata, adenomata, angiomata.
(*b*) Malignant tumours : hypernephromata, carcinomata, sarcomata.

In addition there are new growths of the renal pelvis : innocent tumours—papillomata ; and malignant tumours—carcinomata. Innocent tumours of the kidney are relatively rare, the adenomata being the most common.

Most malignant tumours of the kidney are primary and the commonest is the hypernephroma originally described in 1883 by Grawitz and still known by his name. It was thought by him to be a suprarenal rest but is now considered to be either a malignant adenoma of the kidney or possibly a carcinoma of the renal tubules. It may occur at any age and begins as a solid tumour of the upper pole of the kidney which later undergoes cystic degeneration with areas of necrosis and hæmorrhages. Microscopically it resembles portions of the adrenal cortex. Metastases occur via the blood stream and involve the lungs, long bones, vertebræ, bones of the skull, or indeed almost any organ of the body. The secondary deposits may first draw attention to the condition. In the lungs a large circular opacity resembling a cannon-ball may be seen on X-ray examination. Sarcomata usually occur in children under five years of age and are therefore thought to be congenital in origin.

Signs and Symptoms.— *In children* the first sign is usually a progressive enlargement of the abdomen, pallor, loss of weight, or pressure causing obstinate constipation ; hæmaturia is comparatively rare. The most frequent form of new growth is a congenital sarcoma. The prognosis is extremely bad, though nephrectomy should be performed without delay in the absence of obvious secondary deposits. *In adults* the cardinal symptoms of malignant growths are hæmaturia, pain, and loss of weight. Hæmaturia is generally the earliest sign and is present in over 75 per cent. of cases at some stage. Pain may be intense or merely a dull ache in the back or loin. Renal colic may be simulated by the passage of clots of blood down the ureters. The sudden appearance of a varicocele on the left side may be an initial symptom, as the left spermatic vein enters the left renal vein. The treatment of all forms of renal new growths is purely surgical. In connection with this subject it may be pertinent to mention two important rules of nephrology : (i) the most common cause of hæmaturia in children is some form of glomerulo-nephritis ; in adults over middle age, malignant growths ; and (ii) hæmaturia in an adult should arouse suspicion of a malignant growth until this diagnosis has been disproved.

RENAL CALCULUS

Renal calculi consist of various crystalline or amorphous urinary constituents bound into a mass by a cementing substance. Among the factors believed to contribute to their formation are the presence of an organic nucleus, stagnation of the urine, alterations in its colloid content, and massive excretion of calcium as in parathyroid tumours, vitamin D excess, and bone disease. In size, calculi vary from minute concretions to large single or multiple stones. In rather more than 10 per cent. of cases they are found in both kidneys. Most calculi are of mixed composition but pure stones may occur. Uric acid, calcium oxalate, calcium phosphate, and ammonio-magnesium phosphate are the commonest varieties. Calcium carbonate, cystin, and xanthin stones are also met with. Although oxaluria may accompany calcium oxalate calculi it often occurs independently, following the ingestion of such vegetables as rhubarb, spinach, strawberries, and tomatoes, or it may occur in patients with achlorhydria. Renal calculi occur at all ages but are most common in young male adults.

Symptoms.—Pain, usually lumbar, is by far the most frequent initial symptom. It may be sharp, or a dull ache intermittent or continuous, and in not a few cases may be referred to the region of the unaffected kidney. The attacks of pain may be accompanied by nausea and vomiting. On microscopical examination of the urine, blood and pus are frequently found. In some cases there are definite attacks of gross hæmaturia. When calculi are passing down the ureters, attacks of the most excruciating pain may occur, associated with vomiting ; these attacks are typical and are referred to as *renal colic.* The pain usually starts in the loin or kidney region, and shoots down to the groin or testicle in the most agonising spasms. The patient is doubled up with pain, which may continue with short intermissions for several hours unless morphia be given. The pain then diminishes and passes off, generally to recur some weeks or months later. Cessation of the pain does not necessarily mean that the stone has passed into the bladder but more often that fatigue of the muscular wall of the ureters has set in. Hæmaturia commonly occurs after an attack of renal colic. Bilateral renal calculi may cause destruction of the renal tissue and so give rise to uræmia ; other complications are pyelitis, pyelonephritis, hydronephrosis and pyonephrosis.

Diagnosis.—The typical nature and distribution of the pain, together with blood and pus in the urine, renders the diagnosis in many cases easy. In others the symptoms are less typical and may give rise to confusion with numerous disorders, the most common of which are appendicitis, intestinal obstruction, sacro-iliac disease, lumbago, gall-stones, tabetic crises, or other renal disorders. Radiology, cystoscopy, and urography are invaluable aids to diagnosis.

Treatment.—It is important to remember that most stones are passed spontaneously. The pain of renal colic may be relieved by hot baths or the local application of hot poultices or hot-water bottles to the loins. Copious drinks of hot lemonade, barley water, or weak tea are also of value. If these measures do not suffice, morphia—$\frac{1}{4}$ gr. with or without $\frac{1}{100}$ gr. atropine—should always be given and repeated if necessary. Inhalations of chloroform may be used until the morphia takes effect. Between attacks the patient should lead a quiet life, avoiding sudden exertion of any kind and drinking freely of mineral waters to which either the citrate or bicarbonate of potash may be added. The radical treatment of stones which are not passed spontaneously, and are either causing persistent distress or infection of and damage to the kidney, is surgical removal, though occasional success is claimed for the intraureteric injection of acid and alkaline solvent solutions in appropriate circumstances.

Decubitus Calculi.—Long-continued immobilisation on the back on a level bed or frame, as in the treatment of tuberculous spine or severe rheumatoid arthritis, causes urinary stagnation and increases the tendency to form renal calculi. This can be prevented by giving ample fluids and changing the inclination of the bed through both axes every few hours.

POLYCYSTIC KIDNEYS

This is a comparatively common congenital abnormality occurring in about 1 in 600 autopsies. It is usually bilateral, though generally one

kidney is more affected than the other. It is often familial. Death usually occurs either in early childhood or in middle life. The liver and pancreas are also sometimes the seat of a similar cystic degeneration. The cysts vary in size and number but eventually destroy the normal kidney tissue and lead to death from uræmia. The disease generally remains latent though infrequent attacks of hæmaturia may lead to the discovery of enlarged kidneys. Signs and symptoms of renal insufficiency appear very slowly, and in no other condition is a high blood urea known to persist so long, sometimes for several years, without other signs of renal failure. The blood pressure tends to increase in the later stages. The diagnosis rests on the history of attacks of hæmaturia and the presence of enlarged kidneys, and especially upon the rather characteristic pyelographic appearances. The prognosis is ultimately extremely bad, and there is no treatment other than efforts to maintain a state of compensation for impaired renal function for as long a period as possible, and to observe extra care in avoiding exposure and chills.

A. A. Osman.

AFFECTIONS OF THE JOINTS AND BONES

ARTHRITIS

ARTHRITIS involving one or more joints may complicate infective illnesses such as pneumonia, gonorrhœa, bacillary dysentery and undulant fever. It is often a serious complication in septicæmias, especially those due to streptococci and staphylococci. Tuberculous joints may appear to be primary but are probably always associated with a tuberculous focus elsewhere. Arthritis may also occur in allergic conditions such as serum sickness, as a result of metabolic disturbances such as gout, and in certain nervous diseases such as syringomyelia and tabes.

When, however, all cases of arthritis of known origin are excluded, there remains a very large group where arthritis is the most prominent though not necessarily the only manifestation of disease. Two very frequently encountered types of arthritis fall under this heading and are known as rheumatoid arthritis and osteo-arthritis; and in addition, allied probably to rheumatoid arthritis, there are two relatively uncommon varieties, ankylosing spondylitis and Still's disease. Although in rheumatoid arthritis osteo-arthritic changes may eventually supervene, the two conditions are completely different as regards their age and sex incidence, ætiology, and clinical manifestations, and they accordingly are described separately.

OSTEO-ARTHRITIS

Some degree of osteo-arthritis, particularly in the larger joints, is present in practically 100 per cent. of persons over the age of fifty. Fortunately it often causes little or no disability.

Morbid Anatomy.—Osteo-arthritis may affect any joint, but chiefly the spine, the knees, hips, elbows, and acromio-clavicular joints. The shoulders are less frequently involved. It may sometimes involve one joint only, but usually several are affected, though with varying degrees of severity. The primary changes are erosion and destruction of the cartilage, particularly at pressure points, and thickening of the sub-chondral bone due either to compression or new formation. In advanced osteo-arthritis there is complete destruction of the articular surfaces, and where the bones come in contact they show a dense, hard surface described as eburnation. In addition, around the edges of the joint there are bony projections termed osteophytes. The synovial membrane is only involved secondarily.

Ætiology.—Osteo-arthritis is not a systemic disease with secondary joint manifestations but a primary disease of the joints themselves. Trauma is a frequent cause, and injuries even in relatively early life may many years later produce severe osteo-arthritis. The incidence increases with age and the changes are almost certainly due to "wear and tear" of the articular surfaces. Focal infection is probably unimportant. Abnormal strain on

joints produced by faulty posture or over-weight ultimately results in osteo-arthritic changes.

Symptoms.—These will depend on the joints involved. Disability is usually greatest when the hip joint is affected.

On physical examination movement is often limited owing to the disorganisation of the joint, the presence of osteophytes, and the thickening of the capsule. Marked crepitus can be felt, due to erosion of the articular cartilage. Osteophytes may be palpable as small, hard projections around the edges of the joint. Pain is a very variable feature and symptoms may be absent or negligible even with advanced disease. Patients with osteo-arthritis often find that their pain is much aggravated in cold and wet weather, and is relieved by warmth. The blood sedimentation rate is within normal limits and there is no anæmia. The general health is unimpaired.

Treatment.—From the nature of the disease cure is obviously impossible, but in severe cases considerable relief may be obtained by the use of surgical appliances such as caliper splints. Deep X-ray treatment is sometimes helpful, or in very severe disease of the hip joint, excision of the joint and ankylosis may relieve the pain. When the knees are chiefly involved, if the patient can lose a considerable amount of weight there is less strain on the joints. Sometimes manipulation under an anæsthetic is helpful. Aspirin often gives relief, and its continued use rarely produces unpleasant symptoms. Diathermy and physiotherapy are often of great assistance.

Climacteric Arthritis.—Arthritis is not uncommon in women at the menopause but it is doubtful whether it is due to endocrine dysfunction. It affects chiefly the knees and occurs in patients who are obese. Loss of weight as a result of dieting or thyroid extract often relieves the symptoms. Œstrogenic therapy (*vide* p. 221) is also said to give good results.

Heberden's Nodes.—These are small nodular swellings at the bases of the terminal phalanges. They occur in association with any form of arthritis but most often with osteo-arthritis. They are not uncommon in the absence of arthritis elsewhere.

RHEUMATOID ARTHRITIS

This type of arthritis is sometimes also known as atrophic or infective arthritis. The disease affects mainly females, the proportion being about seven females to one male, and it is most common between twenty and forty. This is in striking contrast with osteo-arthritis, in which males are more often affected, and the incidence increases with advancing years.

Ætiology.—In spite of an enormous amount of research the problem of the ætiology of rheumatiod arthritis remains unsolved. The view that it is due to focal sepsis in teeth, tonsils, or elsewhere has less support than in the past, though there are some features which suggest that the disease is infective in origin. Among these are pyrexia, tachycardia, moderate leucocytosis, increased sedimentation rate, and evidence of general ill-health, such as anæmia. Moreover, histological examination of synovial membrane and periarticular tissues show changes resembling those seen in inflammatory conditions.

If the disease is due to a local focus of infection there are three possible explanations for the development of arthritis: (i) that micro-organisms actually migrate from the focus to the joints—in other words, that the arthritis

is metastatic in origin ; (ii) that toxins formed in the focus of infection are absorbed and produce secondary changes in the joints ; (iii) that the presence of an infective focus produces a " sensitisation " of the tissues, and that rheumatoid arthritis is comparable with allergic manifestations, such as the joint conditions sometimes seen in serum reactions. None of these explanations can be regarded as wholly satisfactory. It is certain that the arthritis is not metastatic and bacteria are very rarely found in either the blood or the joints of rheumatoid arthritis. In favour of an allergic origin is the fact that a considerable proportion of patients with the disease show positive skin reactions to toxic products derived from hæmolytic streptococci.

If proof of the infective origin of rheumatoid arthritis is deficient, there is even less evidence in favour of other hypotheses. Endocrine dysfunction, deficiencies in diet, disturbances of the sympathetic nervous system have all been suggested as causal factors, but there is little or nothing to support any of these views.

In general it may be said that, whatever be the mechanism underlying the development of rheumatoid arthritis, general ill-health, malnutrition, and unhygienic surroundings play an important part as predisposing factors.

Symptoms of Rheumatoid Arthritis.—These vary considerably according to the stage of the disease and its severity. The onset may be somewhat sudden, often with pyrexia, but in such cases a careful inquiry into the history will usually elicit the fact that vague joint symptoms, such as pain and stiffness, had been present for some time before more acute symptoms developed. Much more frequently the onset is insidious, and it is only after several months that the patient is compelled to seek medical advice. As with so many other chronic diseases, spontaneous remissions, partial or complete, are not uncommon.

The symptoms and signs may be dealt with most conveniently under two headings, the condition of the joints and the general symptoms.

Joints.—In rheumatoid arthritis any joint may be affected, but those most constantly involved are the small joints of the hands and feet, more particularly the proximal interphalangeal joints. In addition to these, any or all of the larger joints may show pathological changes.

In the earlier stages of the disease the most prominent symptoms are pain and stiffness, and the latter is most marked when the patient awakes in the morning. On moving the joints the stiffness to a great extent passes off, only, however, to recur after a period of rest. The earliest change is a thickening of the periarticular tissues, associated with variable amounts of fluid in the joint cavity. In the case of the interphalangeal joints there is a characteristic spindle-shaped enlargement, which is usually most obvious in the proximal joints. The skin over the affected joints is often pale, waxy, translucent, and shiny. The temperature of the joints is usually subnormal, and there is profuse local sweating of the palms and soles. When larger joints, such as the knees, are affected, the joint becomes somewhat swollen, and looks even larger than it really is, owing to rapid wasting of the muscles in the neighbourhood. During the more acute stages of the disease the joints are tender on pressure, and although movement is possible it is painful. When definite periarticular thickening has occurred the deformity of the joint persists for long periods, even though pain and tenderness may have disappeared.

In the more chronic cases of rheumatoid arthritis there is great deformity of the joints; although bony ankylosis does not occur, movement may be quite impossible owing to contracture and thickening of the ligaments. In the hands, wrist-drop is common, and ulnar deflection of the fingers is characteristic; similarly, foot-drop may occur. The knees show a great tendency to become acutely flexed.

The synovial membrane is thickened, but the only change in the bones is a rarefaction in the neighbourhood of the affected joints, which renders them unusually translucent to X-rays. In severe and very chronic cases, however, there may be erosion of the joint surfaces, associated with subluxation and disorganisation of the joints, and fibrous ankylosis.

General Symptoms.—Although the most prominent symptoms are referable to the joints, rheumatoid arthritis must be regarded in a broader aspect as a general disease. In nearly all cases there is some pyrexia, which, especially during the more acute stages, may reach 102° F. or higher. The pulse-rate is often persistently raised, even though the patient is in bed, but apart from this there is no evidence of cardiac involvement. The blood pressure is usually low. There is often a moderate secondary anæmia, usually with a definite polymorphonuclear leucocytosis. A raised blood sedimentation rate is always found. The appetite is poor and the tongue furred. Headache and depression are common. Amelioration of the joint symptoms is usually preceded by an improvement in the general health.

Treatment.—Attention to the general health is of prime importance. The patient should be nursed in an airy and well-lighted room, or even better, on an open veranda. In the absence of sunshine ultraviolet light is often beneficial. A good mixed diet with an abundance of fresh fruit and green vegetables should be taken. In addition, wheat germ should be given, as it contains much vitamin B, and cod-liver oil is sometimes beneficial. Blood transfusion is often recommended, especially in patients with considerable anæmia.

Focal Infection.—Extraction of teeth, tonsillectomy, and other operations aiming at eradication of focal sepsis are ineffective if not harmful. Such operations should be confined to those cases where the operation would be regarded as advisable, quite apart from the fact that the patient has rheumatoid arthritis.

Treatment with vaccines, whether autogenous or stock, is disappointing. Any improvement that results is likely to be psychological. Penicillin is as a rule ineffective, but it is perhaps justifiable to give a course of the drug in cases which fail to respond to other forms of treatment.

Protein-shock Therapy.—There is no evidence that this form of treatment produces any permanent amelioration of symptoms. Artificial pyrexia (pyrotherapy) carried out in the Kettering hypertherm is often of value in gonoccocal arthritis but not in rheumatoid arthritis.

Gold Therapy.—During the last ten years gold therapy has become firmly established as the most effective treatment in rheumatoid arthritis. There are numerous proprietary gold compounds which are given intravenously or intramuscularly (Lopion, Myocrisin, Solganal B). The initial dose is 0·01 gm. increasing to 0·1 gm. The injections are given at weekly intervals until a total of 1 gm. has been given. Treatment should then cease for three months before a second course is started. The actual dose and the extent to which it is increased depend on the reaction produced. The aim should be to

give such an amount of the drug as will produce an exacerbation of symptoms lasting twenty-four hours. The blood sedimentation rate is a guide to treatment. Injections must be stopped if toxic manifestations, such as albuminuria, anæmia, agranulocytosis or a falling leucocyte count, rashes, whether erythematous or purpuric, or stomatitis, develop. Diseases of the heart, liver, or kidneys are contraindications to gold therapy; tests of renal function should always precede treatment.

Treatment by Drugs.—Aspirin in 10-gr. doses, especially if combined with 5 gr. of phenacetin or medinal, may give considerable relief. Supposed intestinal antiseptics such as salol and guaiacol are of no value. The patient is usually anæmic and iron should be given in full doses.

General Management.—An essential point in the treatment of rheumatoid arthritis is the prevention of deformity. This object is best attained by ensuring that the joints are kept in satisfactory position during the acute stage of the disease. To avoid wrist-drop and foot-drop, suitable splints must be applied, and it is most important to prevent the knees becoming fixed in a position of flexion. The blood sedimentation rate should be estimated at intervals, as a fall in the rate is an indication of improvement. The most valuable guide as to the activity of the disease is tenderness on pressure over the affected joints. So long as this persists, rest is indicated, but all the affected joints should be gently moved through their full range once every day to prevent the formation of adhesions. When the joint is no longer tender, active movements and massage must be instituted. If deformities such as wrist-drop have occurred, no attempt should be made to improve the position of joints by forcible movement, either with or without an anæsthetic, until local tenderness has disappeared. Any manipulation of joints which are actively inflamed is likely to lead to a serious exacerbation of symptoms.

The problem of the restoration of function in joints deformed by rheumatoid arthritis is mainly one for the orthopædic surgeon. Even in cases which appear hopeless great improvement may result. It must be realised that to a certain extent rheumatoid arthritis is a self-limited disease, the activity of which tends to die out in the course of years, even if completely untreated. In chronic cases a great deal of disability is due rather to lack of function than to organic changes in the joints, and provided there are no signs of active disease, vigorous re-education is advisable. Only too often chronic cases of rheumatoid arthritis are allowed to lie in bed as permanent incurables, whereas active and passive movements, combined with encouragement, will often enable the patient to get about.

Massage, active and passive movements, radiant heat, diathermy, local application of hot paraffin wax, whirlpool and foam baths may all help to accelerate recovery and to restore tone to the wasted muscles.

The outlook in rheumatoid arthritis has improved owing to gold therapy, better orthopædic treatment, and physiotherapeutic measures. In dealing with patients suffering from the disease it is essential, though often difficult, to maintain an atmosphere of optimism.

Still's Disease.—This is a rare disease occurring in children, usually starting between the ages of three and six. It is characterised by a multiple arthritis, which in its characteristics is similar to rheumatoid arthritis. There is also a general enlargement of lymph glands and an enlarged spleen. The disease runs a prolonged course with exacerbations and remissions. The cause of Still's disease is unknown.

PLATE 30

Ankylosing spondylitis. Advanced stage, showing "bamboo spine," calcification of ligaments, osteoporosis of spine and obliteration of sacro-iliac joints. (*From "The Rheumatic Diseases," by Frances Bach, M.D. Cassell*, 1935.)

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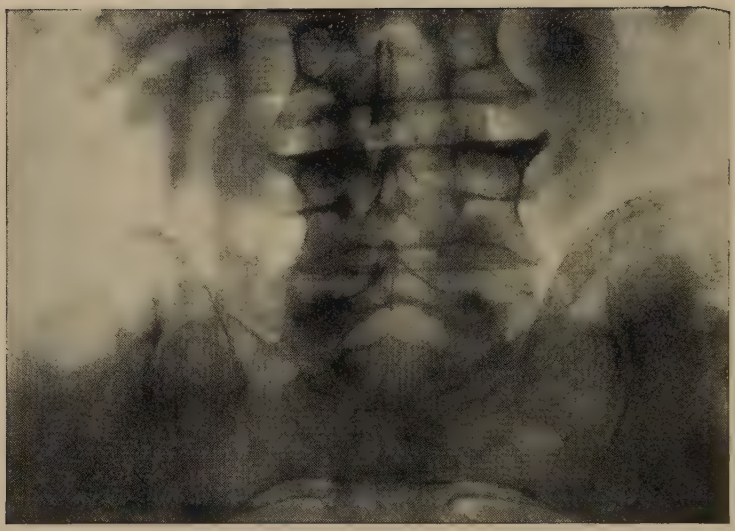

PLATE 31

Spondylitis osteo-arthritica, showing lipping of the bodies of the third and fourth lumbar vertebræ, and normal sacro-iliac joints.
(*From "The Rheumatic Diseases," by Francis Bach, M.D. Cassell*, 1935.)

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Ankylosing Spondylitis

Ankylosing spondylitis, or, as it is sometimes termed, "spondylose rhizomélique," is a relatively uncommon disease. Unlike rheumatoid arthritis its incidence is almost entirly confined to males and its onset is in late adolescence to twenty-five years of age. The main changes are found in the spine and sacro-iliac joints, but sometimes the hip and shoulder joints are involved subsequently.

Nothing is known of the origin of the condition, and there is little evidence that eradication of focal infection is beneficial. From a pathological point of view the chief changes are osteoporosis of the bodies of the vertebræ and calcification of the ligaments of the spine, particularly the lateral and interspinous ligaments. This results ultimately in a completely fixed spine which gives a characteristic X-ray picture, often described as a "bamboo spine" (*vide* Plate 30). It is a striking contrast to the osteo-arthritic spine (*vide* Plate 31). In the latter there is much lipping of the bodies of the vertebræ and no calcification of the ligaments. The spine is usually kyphotic, and in advanced cases the chest becomes fixed, owing to bony ankylosis of the costo-vertebral articulations.

The symptoms of ankylosing spondylitis are pains in the back, spreading down to the arms and legs, striking limitation of movement, and later deformity of the back with varying degrees of limitation of movement in the hips. The blood sedimentation rate is often raised. The condition is usually slowly progressive, and ultimately the patient may succumb to intercurrent respiratory infection.

Treatment with X-ray often produces improvement. During the acute stages rest is indicated. Plasters and spinal supports may prevent spinal deformity. Remissions occur, the disease sometimes becoming arrested spontaneously.

NON-ARTICULAR RHEUMATISM

Aches and pains in the muscles as opposed to the joints are a very common complaint, which causes a vast amount of invalidism and absence from work. The condition is variously described as muscular rheumatism, fibrositis, lumbago, torticollis, neuritis, or pleurodynia. Without doubt some of the cases previously diagnosed as lumbago are due to prolapsed intervertebral discs, while others diagnosed as fibrositis ultimately turn out to have a serious underlying condition, such as spondylitis or secondary deposits in the spine. Symptoms occur most often in males of middle age or over and appear to be precipitated by exposure to wet or cold, and hard or unaccustomed muscular exertion.

One of the most frequent sites of pain is the lumbar fascia and the attachments of the lumbar muscles, when the condition is usually described as lumbago. A similar condition in the muscles of the neck produces torticollis. When the intercostal muscles are affected there is pain on taking a deep breath or on movements of the thorax (pleurodynia). As a rule there is little or no impairment of general health and no pyrexia. The sedimentation rate remains normal. On examination tender nodules are sometimes palpable in the affected muscles, but similar nodules can often be palpated in apparently normal muscles. Without doubt in many cases of so-called fibrositis

the symptoms are an expression of an emotional disorder and are purely psychogenic. "Rheumatism" is also a common complaint among those who wish to shirk unpleasant duties.

Many and varied treatments are advised. It is doubtful if focal sepsis is a cause of fibrositis, but if there is definite sepsis, such as a root abscess, it should be dealt with. Injection of novocaine into any tender nodules detected may give relief. Physiotherapeutic measures such as diathermy or irradiation with infra-red rays and massage undoubtedly do good in most cases. When the condition is wholly or in part psychogenic it is important not to allow physiotherapy to be continued indefinitely.

Myositis Ossificans.—This rare condition is characterised by intramuscular ossification. It usually follows acute or chronic trauma or occupational strain of certain muscle groups, and occurs most commonly in the muscles of the thigh and in the upper arm. Even without interference myositis ossificans following trauma shows a marked tendency to retrogress.

Bornholm Disease (Epidemic myalgia).—In this condition, which may possibly be a virus infection, there is abdominal pain and the muscles, especially those of the abdominal wall, are extremely tender. The onset is sudden, with slight fever, and the patient may appear to be suffering from an acute abdominal emergency. Recovery occurs spontaneously in about a week.

DISEASES OF BONES

Osteitis Deformans (*Paget's Disease*).—The onset is very gradual and symptoms seldom arise before middle life. The striking features are a progressive enlargement of the skull together with a symmetrical thickening and bowing of the long bones, more particularly the femur and tibia. The increase in the size results from formation of new bone beneath the periosteum. The disease is often associated with arteriosclerosis, but nothing is known of its causation.

Headache is a frequent symptom and there is sometimes pain and tenderness in the affected bones, which are liable to fracture with slight trauma. The disease is slowly progressive and is not in itself fatal, though death is liable to occur from intercurrent infections and from sarcomata arising in the affected bones. No treatment appears to modify its course.

Osteogenesis Imperfecta.—This rare condition is congenital, with a tendency to occur in families. Survival to adult life is unusual. The disorder is primarily nutritional, and the bones, particularly the long bones, are unduly fragile; the cortex of the bone is thin and deficient in calcium. Spontaneous fractures are the most prominent symptom and lead to marked deformity and shortening of the limbs. Often there is a blue coloration of the sclerotics. There is no treatment beyond the exercise of care in avoiding trauma. If the patient reaches adolescence, spontaneous improvement occurs.

Osteomalacia.—This disease is almost confined to the female sex and usually occurs between the ages of twenty and thirty. It is often associated with pregnancy; defective hygienic conditions and an unsatisfactory diet are also predisposing causes.

The bones affected are the long bones, spine, ribs, and pelvis. The amount of calcium in these is much diminished, and as a result the bones are softer and more fragile than normal. Spontaneous fracture is common, and this

may be the first obvious symptom of the disease. In advanced cases great deformity results from the softness of the bones ; this is specially true of the pelvis, in which the sacrum is pushed downwards as the result of the weight of the body while the acetabula are driven inwards by the heads of the femurs.

The course of osteomalacia is very variable but the disease is usually progressive, and death eventually results from intercurrent respiratory infections. Further pregnancies should be avoided and a diet rich in calcium and phosphorus should be taken. Cod-liver oil is sometimes beneficial.

Multiple Myelomatosis.—In this rare condition the bone-marrow is invaded by multiple neoplasms of sarcomatous type. Spontaneous fractures are very common. In many of the cases the urine contains Bence-Jones protein. This can be demonstrated by heating the urine ; when the temperature reaches about 50° C. the protein coagulates with the formation of a turbid precipitate : if the heating is continued to the boiling point the coagulated protein becomes redissolved.

Achondroplasia.—This disease originates during fœtal life and affects mainly the bones which develop from cartilage. Those most commonly involved are the long bones, the pelvic bones, and the base of the skull. Growth is stunted, and achondroplasiacs who reach adult life are seldom over 4 ft. in height ; the legs and arms are very short in comparison with the development of the trunk ; the face appears small, but the cranial vault is normal in size. Although the bones are short and bowed, they are strong and do not fracture readily. Intelligence is normal, and the subjects of the disease often live in good health to an old age. The fingers tend to be equal in length. Treatment is ineffective.

Hypertrophic Pulmonary Osteo-arthropathy.—This cumbersome name is given to the condition of " clubbing " in the fingers and certain bony changes which occur in bronchiectasis, empyema, pulmonary abscess, bronchial carcinoma, chronic phthisis, subacute bacterial endocarditis, and congenital heart disease.

Clubbing of the fingers is very common in all the above-mentioned conditions and a similar change also occurs in the toes. The terminal phalanx is swollen and often somewhat cyanosed ; the finger-nail is curved, and at the base of the nail the skin has a shiny, tense appearance. In marked cases the tips of the fingers are expanded in both their anteroposterior and lateral diameters. The clubbing is nearly always symmetrical. X-ray examination shows no obvious changes.

In addition to clubbing there is occasionally enlargement of the bones of the extremities, particularly of the hands and feet, and sometimes osteo-arthritic changes in the joints. Whereas clubbed fingers are very common, the fully developed condition of pulmonary osteo-arthropathy is exceedingly rare. Whether the changes are due to interference with tissue nutrition, which results from prolonged venous congestion, or whether there is some specific toxæmia remains undecided.

Generalised Osteitis Fibrosa is discussed under Disorders of the Parathyroid (*vide* p. 216).

J. J. Conybeare.

DISEASES OF THE NERVOUS SYSTEM

THE GENERAL SYMPTOMATOLOGY OF ORGANIC NERVOUS DISEASES

THE central nervous system, enclosed within the bony framework of skull and vertebral column, is inaccessible to direct observation; hence, with the exception of the head of the optic nerve which lies open to view in the fundus of the eye, the nervous system cannot be investigated by the clinical methods of inspection, palpation, or percussion, upon which we so largely depend in the diagnosis of diseases of the thoracic and abdominal viscera. Therefore the recognition and clinical localisation of disease within the nervous system depend upon the observation and interpretation of signs of disordered activity in tissues innervated by this system. In short, the diagnosis of nervous diseases is more largely a matter of applied anatomy and physiology than is often the case with diseases of other systems.

The Functional Reactions of the Nervous System to Disease

The activities of any part of the nervous system which is directly involved in a focus of disease or injury may be disordered in either of two ways. They may be diminished or abolished on the one hand, or they may be stimulated to an excessive degree on the other. Thus a lesion of the cerebral motor cortex may by destruction of nerve cells produce motor paralysis, or by stimulation give rise to a focal or Jacksonian convulsion. Both effects may be combined; a focal fit being followed by motor weakness. It is usual to speak of the two orders of symptoms so produced as *paralytic* and *irritative* respectively. Again, while the nervous system shows a high degree of local specialisation of function, yet normally it acts as a whole, and damage to any one part of it may be followed by disorder of function in regions left untouched by disease. Such disorders may be said to be indirectly produced and, like those directly caused, are of two orders. For example, when a hæmorrhage occurs within a cerebral hemisphere and tears up the pyramidal fibres as they course down through the internal capsule, the direct result of the lesion is a hemiplegia. But there is also a sudden loss of consciousness which may persist for some days. A predominant part in the production of this coma is played by "shock" or "diaschisis," the functions of both cerebral hemispheres being temporarily abrogated on the sudden development of a gross destructive lesion within their substance. This shock passes off, all parts of the cerebrum resuming activity except that actually destroyed by the hæmorrhage, while the direct result of the destruction, the hemiplegia, remains as a more or less permanent residuum.

But the hemiplegia, at first flaccid, in course of time becomes spastic, that is, the muscles which have lost voluntary power begin to develop an excessive tonus, show exaggerated tendon reflexes and the phenomenon of

clonus. In certain circumstances they may even develop involuntary movements. All these phenomena indicate an excessive activity of parts of the nervous system not destroyed by the lesion, but rather released from a control normally exercised over them by the neurones now destroyed. Thus there are four groups of symptoms of disordered action of the nervous system :—

Directly produced . . .	" Paralytic "	symptoms.
	" Irritative "	,,
Indirectly produced . . .	" Shock "	,,
	" Release "	,,

It will be readily appreciated that of these, symptoms due to shock and irritation tend to be transient, while those resulting from destruction or release may persist indefinitely. In many chronic nervous diseases, such as paralysis agitans, residual hemiplegia, and double athetosis, release symptoms may be in the forefront of the clinical picture, paralytic manifestations taking the second place.

There are other factors governing the impairment or dissolution of function in diseases of the nervous system, to some of which we may summarily refer. Thus acutely produced lesions are apt to cause more intense and extensive disorders of function than similarly localised and extensive lesions of gradual development. Again, when a high-grade function is undergoing dissolution from the action of a disease process, its most recently and finely developed aspects are earlier and more severely impaired than its older and simpler components. Thus in residual hemiplegia the skilled movements of the fingers are more severely impaired than the simpler movements in the proximal parts of the upper limb, and recover less rapidly and completely than the latter, Again, in that complex motor function, articulate speech, the power of expressing thought in a foreign language may be lost in an individual who retains this power in his native tongue. Similarly, a comparable graded dissolution of sensory function may result from appropriate cerebral lesions.

Again, we cannot regard the central nervous system as entirely independent of the other tissues of the body. Its activity is, for example, delicately responsive to variations in the quality and quantity of its blood supply. The nerve cell in particular is extremely sensitive to oxygen deprivation, being stimulated at first and then paralysed as the oxygen supply drops below normal. The convulsions of asphyxia and those which may accompany sudden profuse hæmorrhage into the peritoneal cavity are examples of the hyperexcitability developed by the cell at a certain level of oxygen starvation. The coma which ensues indicates abolition of function from more severe oxygen want.

The Structural Reactions of the Nervous System to Disease

In what is primarily a clinical account of nervous diseases the structural reactions may be very briefly described. The complete nervous system may be regarded as consisting of vascular, supporting, and parenchymatous elements. In a given case of nervous disease any one of these may be primarily affected, the others being secondarily involved, and the resulting lesion will be

the combined reaction of all three to the pathogenic agent. Thus a primary parenchymatous degeneration will be followed by a secondary glial proliferation and by a phagocytic activity of certain glial elements.

The nerve cell studied by the Nissl staining method shows three main types of reaction. The most familiar of these is known as *chromatolysis* and corresponds to the cloudy swelling of other cells : the cell body swells, the granules in the cytoplasm undergo some measure of dissolution, and the nucleus becomes eccentric. In mild degrees these are reversible changes. In some intoxications there arises what is known as *chronic cell change*, in which both cell body and nucleus shrink, the granules disappear, and the cell may die. This change results from ischæmia. We also see *acute necrosis* in which cell and nucleus swell, granules and neurofibrils disappear, and the entire cells take on a homogeneous appearance.

Dead neurones undergo dissolution and the products of destruction are removed by phagocytes. A typical change in white matter within the central nervous system is demyelination, the axis cylinders remaining more or less intact.

SYMPTOMS OF DISEASE OF THE MOTOR SYSTEM

The motor system may be taken to consist of three main components : (i) the pyramidal or upper motor neurone extending from the cerebral motor cortex to the anterior horn cells of the opposite side of the spinal cord ; (ii) a complex group of extra-pyramidal neurones, comprising numerous masses of grey matter in the cerebral hemispheres and in the brain stem, with the fibre systems arising in them and extending in one or more links to the ventral horn cells of the cord ; and (iii) the lower motor neurone, which includes the motor nuclei of the cranial nerves and the anterior horn cells of the spinal cord.

The last named is " the final common path " to the skeletal muscles, and upon it play the upper motor and extra-pyramidal systems of neurones and also the central ends of the afferent limbs of the spinal reflex arcs.

The Upper Motor Neurone may be regarded as the sole path for the conduction of volitional motor impulses and as exercising control over the extra-pyramidal motor system ; therefore damage or destruction of this neurone has a dual effect. There is an impairment or loss of voluntary movement, a directly produced phenomenon, and an increase of muscle tone and of tendon reflexes, with a qualitative change in the plantar response. The latter are release phenomena, and result from the uncontrolled activity of extra-pyramidal motor mechanisms which still continue to play upon the lower motor neurone. The condition of spastic paralysis resulting from disease of the upper motor neurone is seen in its fullest expression in residual hemiplegia. It is possible that some elements in the positive symptoms that are seen in residual spastic hemiplegia follow upon the interruption of paths descending from the frontal cortex other than the pyramidal system : that is, that the complete picture of spastic hemiplegia involves the interruption of two descending neurone systems, pyramidal and extrapyramidal. The loss of voluntary movement in hemiplegia affects unilateral movements only, and these unequally. Thus in the upper limb, which is usually more affected than the lower, movements of the fingers and hand are most impaired. In the leg the movements of dorsiflexion and of flexion are more profoundly impaired than those of plantar flexion and extension. In the face, the movements of

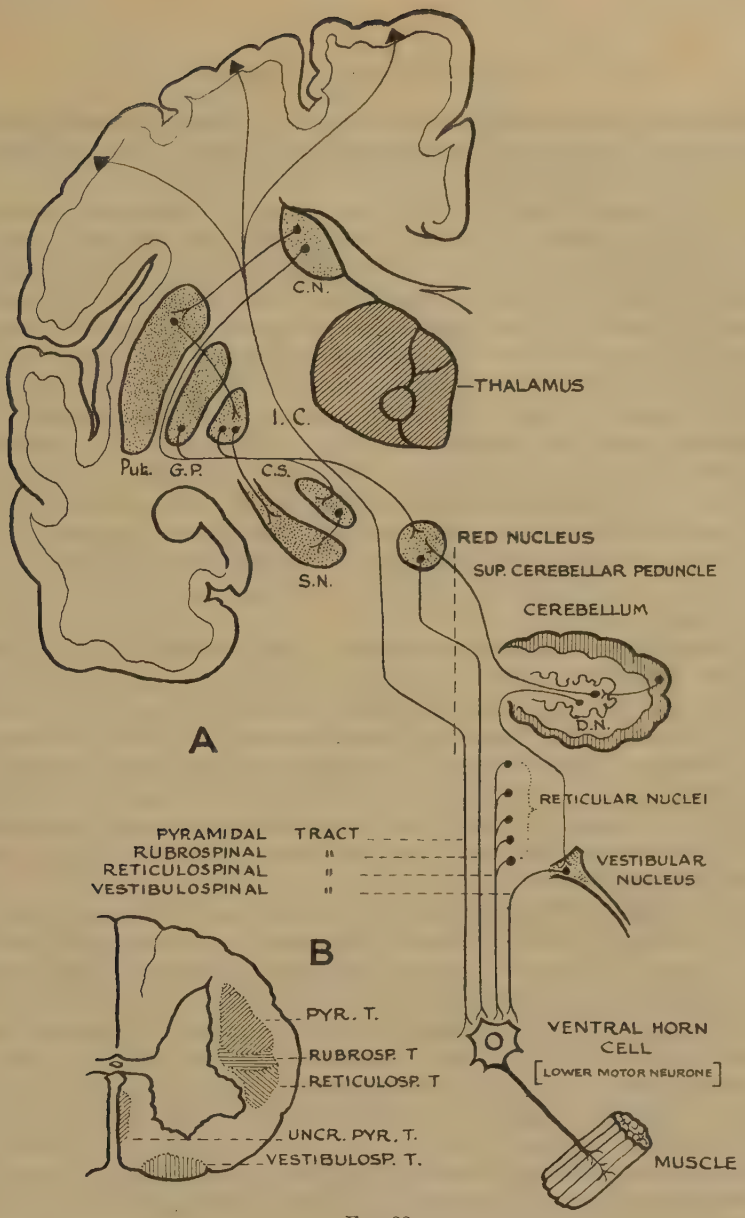

FIG. 23

A and B. The Motor System.

A.—The cortico-spinal or pyramidal tract arises in the cerebral cortex of the ascending frontal convolution and the region immediately anterior to it, and, traversing the internal capsule and brain-stem, decussates in the medulla. It then runs in the lateral column (see B) of the spinal cord to terminate in the grey matter of the ventral horn around the motor cells. The various nuclei which are included in the extrapyramidal system are indicated by stippling. The paths which arise in them include the vestibulo-spinal tract, originating in the vestibular nucleus, and running down in the ventral column of the cord. The small rubrospinal tract which, arising in the red nucleus, immediately decussates and comes to take position in the cord ventral to the pyramidal tract. The reticulo-spinal tract which, arising in scattered nuclear masses in the pons and medulla, also runs down in the lateral column of the cord ventral to the rubrospinal tract. The fibres of all these paths ultimately turn into the grey matter and form synaptic junctions with the ventral horn cells.

The short tracts between the various components of the extrapyramidal system are also indicated: C.N., caudate nucleus. D.N., dentate nucleus. C.S., corpus subthalamicum. G.P., globus pallidus. I.C., internal capsule. Put., putamen. S.N., substantia nigra.

The extrapyramidal system is sometimes spoken of as "the old motor system" in contradistinction to the "new motor system" which comprises the cortico-spinal system.

B.—Transverse section of the cord, showing the relative positions occupied by the various motor tracts.

the lower half are alone involved, while the tongue is protruded towards the paralysed side. The trunk muscles commonly escape, as do the movements of deglutition and mastication.

The hypertonus or spasticity also has a selective incidence, developing in the flexors and adductors of the upper and in the extensor and plantar-flexors of the lower limb. Thus the spastic arm goes into flexion and adduction, the spastic leg into extension and adduction. When spasticity is sufficiently developed not only are the tendon jerks increased but patellar and ankle clonus may be present. Also under certain conditions involuntary tonic spasm invades the muscles leading to changes of attitude in these, which are spoken of as "associated reaction." Finally the normal reflex movement of plantar-flexion of the hallux on stroking the sole of the foot is replaced by one of dorsiflexion, the so-called extensor or Babinski response. This response is accompanied by reflex contraction of all the limb flexors, which in certain cases of paraplegia may develop into a powerful flexor spasm of the limb. The abdominal reflexes also disappear in upper motor neurone lesions. In lesions of the spinal cord involving both pyramidal tracts a condition of spastic paraplegia results.

The Extra-pyramidal Motor Neurones.—These include the corpus striatum, red nucleus, substantia nigra, and other deeply seated masses of grey matter in the brain, and the short and descending paths arising in them. The characteristics of disease of this complex system are an absence of true paralysis and the presence of disturbances of muscle tone (Parkinsonian rigidity), and of involuntary movements (athetosis, tremor, choreiform movements). In uncomplicated lesions of this system the reflexes undergo no qualitative change. The most familiar example of an extra-pyramidal symptom-complex is paralysis agitans, or Parkinson's disease.

The Lower Motor Neurone.—When this neurone is destroyed by disease the skeletal muscle is cut off from all functional connection with the nervous system. There is a degree of paralysis proportionate to the degree of denervation, a loss of reflex muscle tone and of the tendon reflexes, followed by muscular atrophy which may proceed to complete loss of contractile substance in the affected muscles in which secondary fibrosis and deformity finally ensue. In addition, the electrical excitability of the muscle alters and finally disappears (reaction of degeneration, total loss of excitability).

The Cerebellar System.—Although, strictly speaking, this system should be included amongst extra-pyramidal motor mechanisms, it is usual to deal with its symptomatology separately. The essential clinical result of a loss or impairment of cerebellar activity is the development of a gross disturbance of co-ordination in voluntary movement, the so-called cerebellar ataxy, and hypotonia. There are no true paralyses and no qualitative changes in the reflexes. A description of these disturbances of movement will be dealt with under the appropriate heading (*vide* p. 567).

SYMPTOMS OF DISEASE OF THE AFFERENT NERVOUS SYSTEM

The afferent nervous system includes *sensory* and *non-sensory* components. The latter, which is not less important than the sensory component, includes the afferent links of numerous reflex arcs. The grey matter in which

lie the synapses of these arcs is situated at all levels of the spinal cord and brain stem, and the impulses which traverse the arcs do not influence consciousness. The spinal arcs subserve the tendon reflexes and certain reflex movements which underlie the co-ordination of movement. The long arcs which pass up to the brain stem are predominantly concerned in the maintenance of muscle tone and in the regulation of posture. The spino-cerebellar tracts form part of this non-sensory afferent system. The loss of muscle tone and of tendon reflexes, which are amongst the cardinal signs of tabes dorsalis, depend upon a lesion of certain of these non-sensory afferent fibres as they lie in the root entry zone of the posterior white columns of the cord. Disappearance of the tendon reflexes, when not due to paralysis of the muscle concerned, depends upon an interruption of the afferent limb of the arc either in the mixed peripheral nerve, the posterior spinal root, or in the intramedullary part of the latter as it lies in the posterior column of the cord.

The Sensory System, like the motor system, consists of a chain of neurones extending from the periphery to the highest sensory centres in the thalamus and cerebral cortex.

The mixed peripheral nerve contains fibres underlying every aspect of sensibility, both cutaneous and deep, hence impairment or loss of all modes of sensation follows a peripheral nerve lesion, and localisation of the lesion depends upon the determination of the topography of the area of altered cutaneous sensibility. There are four groups of cutaneous nerve fibres and nerve endings. They subserve tactile, painful, and thermal (hot and cold) sensibility. Although the neurones of all four groups run together in the peripheral nerve, each group has its own special anatomical and physiological properties. The power of localising the skin region stimulated by tactile, thermal, or painful stimuli, and of discriminating two simultaneous stimuli from a single stimulus, is probably a resultant of the anatomical grouping of the sensory end-organs in the skin. It seems likely that the physiological cutaneous sensory unit is comprised by all the cutaneous end-organs innervated by a single dorsal root fibre, and is not, as has hitherto been supposed, the single sensory end-organ. Each such end-organ has a multiple innervation, and not less than two nerve fibres subserving the mode of sensibility peculiar to the end-organ enter each of the latter, while in the case of tactile and thermal forms of sensibility a nerve fibre belonging to the pain system also innervates it.

It is the presence of the last-named fibre that gives rise to pain when a tactile end-organ in the skin is subjected to very strong stimulation.

Under normal conditions it must be rare indeed for less than several groups of sensory end-organs to be stimulated at one time, and the capacity for localising stimuli may be a resultant of the simultaneous stimulation of spatially separated end-organs. It is not a function of a special type of end-organ or nerve fibre.

The Central Sensory Paths.—On reaching the spinal cord the sensory fibres undergo a regrouping according to the modes of sensibility they subserve, and travel up in the cord in special paths. Thus impulses underlying tactile sensibility and the sense of position travel up in the original peripheral neurone in the uncrossed posterior white column as far as the posterior column nuclei of the medulla oblongata; here they end, and the second sensory neurones arise, crossing the midline as the arcuate fibres in the decussation of the fillet (sensory decussation), and then turning upwards as

the medial fillet to traverse the pons and midbrain, end in the thalamus. The fibres carrying impulses underlying painful and thermal sensibility end

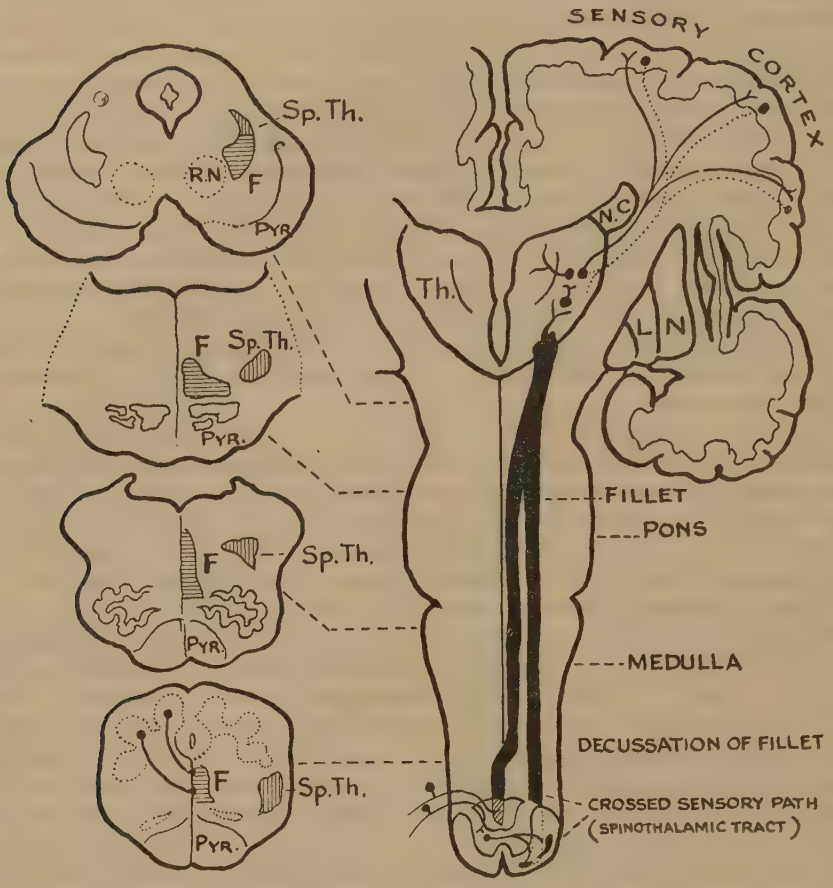

FIG. 24

THE CENTRAL SENSORY PATHS

On the right the sensory pathway is represented in its longitudinal course. On the left a series of transverse sections indicate the positions occupied by the components of the sensory path at the different levels of the brain stem. The uncrossed sensory path runs up in the dorsal white column, its fibres terminating in the dorsal column nuclei of the medulla (nuclei of Goll and Burdach). The path then decussates (decussation of the fillet) and runs up as the medial fillet to the thalamus. The crossed sensory path travels upwards in the lateral column (lateral spino-thalamic tract) and in the ventral column (ventral spino-thalamic tract). These two meet in the medulla and run up together in the lateral region of the medulla and pons, gradually nearing the fillet and finally becoming continuous with it in the midbrain. The entire sensory pathway reaches the thalamus. Thence it divides, one component passing to the main thalamic nucleus, another passing to the sensory cerebral cortex. In dotted lines is represented a cortico-thalamic tract which, so it has been supposed, transmits cortical control of the thalamic component of the sensory mechanism. (Modified after Head and Holmes.) Th., thalamus. N.C., caudate nucleus. L.N., lenticular nucleus. Sp. Th., spino-thalamic tract. Pyr., pyramidal tract. F., Fillet.

in the posterior horns of the side on which they enter the cord, the second neurone crossing the midline to travel up through cord and brain stem in the lateral regions of both, to reach the thalamus with the medial fillet. We thus

have uncrossed and crossed sensory paths in the cord, and in the brain stem two sensory paths, now both crossed, which finally meet in the lateral nucleus of the thalamus. Here the sensory path undergoes a final rearrangement. Impulses underlying the affective aspects of sensibility, particularly pain and thermal sensibility, pass to the essential nucleus of the thalamus, where it is possible that they reach consciousness to form the basis of the corresponding sensations. Those underlying tactile sensibility, and the discriminative aspects of sensibility, pass to the cerebral sensory cortex which is situated mainly in the post-central convolution.

In general, a cerebral or brain-stem lesion involving the sensory pathways produces a crossed hemianæsthesia. In the case of cortical lesions, thermal and painful sensation are little if at all affected, and the characteristic disturbance is an inability to localise cutaneous stimuli, especially tactile stimuli, and a defective appreciation of the size, shape, and texture of objects held in the affected hand (astereognosis). The characteristics of sensory loss from lesions at lower levels within the central nervous system will be dealt with under the appropriate headings.

Inco-ordination of Movement.—The disorders of voluntary movement known as ataxy, or inco-ordination, require brief mention here, as they arise in one of two ways. In lesions of the cerebellum or of the cerebellar fibre system a form of ataxy may develop which has been mentioned above as cerebellar ataxy. This ataxy is not dependent upon any disturbance of the sensory nervous system and is not aggravated when the patient is deprived of vision.

On the other hand, any lesion in spinal cord, brain stem, or cerebral hemispheres which interrupts the sensory impulses conveying the sense of position and the appreciation of movement will produce what is known as a sensory ataxy. Perfect co-ordination requires accurate information from the muscles as to their degree of contraction, and thus as to the position of the limbs, trunk, and head. If this information be not forthcoming, control of movement is impaired or lost and ataxy results. The lack of this information may be compensated in a great measure by vision, but if the patient's eyes be closed this compensation is lost and the maximal degree of disorder of movement is produced. The most familiar example of a sensory ataxy of this order is seen in tabes dorsalis, where the sensory fibres underlying the relevant forms of sensibility are degenerated in the posterior columns of the spinal cord. When the lower limbs are the seat of this disorder the typical tabetic ataxy of gait and stance results, and is aggravated when the subject shuts his eyes, a procedure which is the basis of Romberg's test.

In the case of the upper limbs the contrast between the two forms of ataxy, cerebellar and sensory, is also readily observed. The so-called intention tremor of the arms is an example of the former variety, and is not aggravated when the subject's eyes are shut. When the patient is asked to touch his nose with his finger with his eyes closed, the limb deviates on its way but reaches the nose correctly. In the sensory ataxy of tabes, however, the sense of position of the limb being impaired, the subject's hand wanders and fails to reach the desired objective unless the aid of vision be forthcoming.

Electrical Reactions of Muscle

A healthy muscle in normal functional connection with the nervous system responds by contraction when its motor nerve is stimulated by the

faradic (interrupted) or the galvanic (continuous) current. The muscle fibres themselves are responsive to the make and break of the continuous current but are inexcitable by the interrupted current. The situation at which the application of the stimulating electrode in both forms of current gives the maximal response is the point at which the motor nerve enters the belly of the muscle, the so-called "motor point." The faradic current is obtained from an induction coil, and when applied in sufficient strength provokes a muscular response which persists during the passage of the current. The response to the galvanic current, on the other hand, is restricted to the moments at which the current is made and broken.

Abnormalities in electrical reaction may consist in simple quantitative alterations in excitability or in qualitative changes. Thus general hyperexcitability to both forms of current is found in tetany, while hypoexcitability or loss of excitability to both forms of current is present in disuse atrophy of muscles and in the muscular dystrophies.

In lower motor neurone lesions qualitative changes are found. When a muscle is denervated and the motor nerve fibres have degenerated, the *reaction of degeneration* is present. This consists in a loss of excitability to the faradic current and in an altered response to the galvanic current. Of this alteration to the galvanic current the essential features are a lowering of the threshold of stimulation and a peculiar sluggishness of contraction which is readily visible, the contraction wave sometimes passing slowly along the muscle.

THE REFLEXES IN DIAGNOSIS

The clinical study of the reflexes is of the greatest possible importance in the diagnosis of nervous diseases, for while considerable disturbances of motor and sensory function may, as in the numerous clinical pictures of hysteria, coexist with a nervous system free from discoverable disease, qualitative alterations in the reflexes invariably mean organic disease of this system, and in the initial stages of many such diseases diagnosis may turn entirely upon the state of these reflexes.

Variations in the reflexes may also occur as transient phenomena in certain intoxications and during epileptiform seizures.

The reflexes which are of importance clinically fall into three groups: the tendon reflexes (tendon jerks), the cutaneous reflexes, and the Babinski or "extensor" type of plantar response.

The Tendon Jerks are true spinal reflex reactions and are present in all healthy persons. Under emotional stress, in the psychoneuroses and in some debilitated persons, they may undergo a general increase in briskness, but in these circumstances all the tendon jerks in upper and lower limbs and on both sides are equally affected. An increase in the tendon reflexes in a single limb or in the limbs of one side invariably indicates organic disease. In some normal individuals the tendon reflexes in the upper limbs may be difficult to elicit, while in small children and aged persons a similar difficulty may attend the attempt to obtain an ankle jerk. But with this exception the knee and ankle jerks should always be obtainable. "Reinforcement" may be necessary to elicit them, and this is achieved by asking the subject to clench his fists or to make a sustained and forceful voluntary contraction of muscles not under investigation for the reflexes. In disease of the upper motor neurone the

tendon jerks undergo considerable increase and the phenomenon of clonus may develop in spastic legs; ankle clonus when the foot is dorsiflexed by the examiner, and patellar clonus when the patella is depressed forcibly. In lesions of the lower motor neurone the tendon jerks are diminished or abolished in the affected muscles. In slight lesions this change may be the most striking physical sign, appearing before there is much muscular weakness or wasting. A similar change is seen in muscular diseases, *e.g.*, in muscular dystrophy.

A selective change in certain tendon reflexes may have a localising value in focal lesions of the spinal cord. The segmental localisation of the tendon reflexes employed clinically is given in the following table :—

Biceps brachii	5 to 6 Cervical segments.
Triceps	6 to 7 ,, ,,
Supinator (Brachioradialis)	6 ,, ,,
Knee	2 to 4 Lumbar ,,
Ankle	1 to 2 Sacral ,,

The Cutaneous Reflexes employed in clinical examination are the epigastric and abdominal and the cremasteric reflexes. These generally disappear in all lesions of the upper motor neurone at levels higher than that of their segmental spinal localisation, persisting unchanged in lower motor lesions unless the muscles engaged are themselves paralysed. In healthy persons, stroking the sole of the foot evokes a plantar flexion of the great toe, the so-called " flexor " or normal type of plantar response. This also is a cutaneous reflex and, like those mentioned above, disappears in lesions of the upper motor neurone, being, however, replaced by a new type of plantar response which is not strictly a cutaneous reflex, although commonly described as such.

The Extensor or Babinski Type of Plantar Response which replaces the normal or flexor type of plantar response is a physical sign of the utmost importance in clinical diagnosis. When present as a permanent phenomenon it invariably indicates structural change in the pyramidal system of fibres, that is, in the upper motor neurone. It may in any given case be the only unequivocal sign of such change, but even when thus occurring as an isolated abnormality its significance is unmistakable. As we have mentioned, it may occur transiently in epileptiform seizures (in eclampsia, uræmia, epilepsy, Jacksonian fits), and in certain intoxications without associated convulsions (delayed chloroform poisoning, acute yellow atrophy of the liver, cholæmia, and inconstantly in morphia, hyoscine, and barbiturate poisoning).

The most striking feature of the reflex response is a dorsiflexion of the great toe, generally with an associated dorsiflexion and fanning of the other toes. There is also, however, a constant reflex contraction in all the limb flexors. This may be so slight as to require palpation for its detection, or so violent (in certain severe paraplegias) as to constitute a powerful flexion spasm of the whole limb. The response is most easily and constantly elicited by stroking with the tip of the finger or with the point of a pencil *the outer margin of the sole.* In conditions of severe spastic paralysis of a leg, however, it may be obtained by pricking or pinching the skin almost anywhere over the whole limb, and also by pressure over bones and muscles over a similarly wide area. Therefore the response is not strictly plantar or purely cutaneous. It is homologous with the nociceptive flexion reflex in the hind limb of the spinal animal (Sherrington).

THE CEREBROSPINAL FLUID

The cerebrospinal fluid is secreted by the choroid plexuses of the lateral, third, and fourth ventricles. It leaves the ventricular system by way of the foramina of Majendie and Luschka (median and lateral apertures) in the roof of the fourth ventricle, and passes into the basal cisterns of the subarachnoid space. Thence it flows through the opening between the tentorium and the brain stem up over the cerebral hemispheres, and also through the foramen magnum into the spinal theca. Finally, it is absorbed into the blood stream. This it reaches by means of tiny villous processes which arise in the arachnoid in the neighbourhood of the dural sinuses. The villi cross the subdural space and penetrate the fibrous dural walls of the sinuses, projecting into the lumen. It is possible that some absorption may occur in a similar manner in the spinal subarachnoid space, but the main channels lie in the skull.

The main function of the fluid is probably mechanical, namely, that of providing a water cushion for the brain and spinal cord. It may also carry off degeneration products which flow into it from the perivascular spaces of the brain. It is probable that when secreted it contains neither cells nor protein, these being added to it in the course of its circulation.

Composition.—It is a clear, colourless saline fluid ; on lumbar puncture it is found to be under a pressure of from 60 to 150 mm. of water. The total quantity is approximately 130 c.c. As obtained from the theca it contains from 2 to 5 lymphocytes per cubic millimetre, 0·02 to 0·04 per cent. protein, 0·05 to 0·08 per cent. glucose, and 0·7 per cent. chlorides. Of the protein content, albumin predominates, being always in excess of the globulin fraction, even when both are increased under pathological conditions. The pathological changes characteristic of various diseases are described under the appropriate headings.

Changes may occur as the result of an altered secretion by the choroid plexuses, and in this respect the fluid follows very closely the composition of the blood plasma. But a fluid which is normal on secretion may be altered as it circulates in the subarachnoid space, and it is with such an alteration that we are concerned in acute leptomeningitis.

DISEASES OF THE CEREBRAL MENINGES AND HYDROCEPHALUS

The cerebral meninges may be the seat of inflammatory processes or of new growth formation, the former being the more common, especially in the case of the pia-arachnoid. It is probable, however, that tumour development in the meninges is not so rare as was formerly supposed. The so-called meningioma of the brain arises from arachnoidal cells lying in the substance of the dura mater, while infiltration of the pia-arachnoid by glioma, sarcoma, and secondary carcinoma also occurs ; such infiltration is frequently microscopic and gives rise to symptoms resembling those of meningitis.

Acute Leptomeningitis

Owing to the feeble bactericidal powers of the cerebrospinal fluid and to its free circulation throughout the extensive subarachnoid space, an acute

infective leptomeningitis often leads to a rapidly fatal issue. When death does not ensue, however, the coagulation of inflammatory exudate in the basal cisternæ and the resulting formation of adhesions interfere with the circulation and absorption of the cerebrospinal fluid, and thus lead to the development of internal hydrocephalus. However, since the introduction of sulphonamide therapy this sequel is much less often seen than formerly.

Ætiology.—Acute leptomeningitis is almost invariably secondary to a focus of infection outside the nervous system. The sole probable exception is pneumococcal meningitis, and this not constantly so. Meningococcal meningitis (cerebrospinal fever), formerly regarded as a primary meningitis, is now thought to be a secondary invasion of the subarachnoid space from a primary infection of the nasopharynx. An acute leptomeningitis may be set up by the pyogenic cocci, including the gonococcus, and by the tubercle, typhoid, anthrax, and influenzal organisms. In exceptional instances other organisms may be involved.

The special forms of acute meningitis are discussed under the headings of the infections concerned, but some general observations on the nature, morbid anatomy, and symptomatology of the meningeal reaction may appropriately be given here.

Morbid Anatomy.—Although the inflammatory reaction in the meninges varies somewhat in appearance in accordance with the infecting organism concerned, its general features are more or less constant. The pia-arachnoid becomes intensely hyperæmic, and in exceptional cases multiple small hæmorrhages may occur in its meshes. It also becomes œdematous and cloudy, and as fibrinous exudate is poured out it assumes a thickened gelatinous appearance. In the suppurative forms the fibrinous exudate soon becomes purulent. The process is usually most intense at the base of the brain, but as the exudate increases it tends to spread laterally along the Sylvian fossa and fissure (lateral sulcus) on to the convexity of the hemispheres, where it lies in the hollows between the convolutions, spreading in all directions from the Sylvian fissure. In non-suppurative tuberculous meningitis the spread of infection and the development of tubercles follow the same lines. Changes of the same order occur in the superficial layers of the brain underlying the meninges, namely, serous exudation, minute hæmorrhages, and small foci of encephalitis and hyperæmia.

The Cerebrospinal Fluid.—The acute meningeal reaction reveals itself not only in the structural change noted above but also in alterations in the composition of the cerebrospinal fluid. The nature and severity of the meningeal reaction may be determined from the examination of the cerebrospinal fluid, and therefore the procedure of lumbar puncture is a diagnostic method of the greatest value in acute meningitis.

The essential features of the meningeal reaction as betrayed by this fluid are as follows : the cellular content is greatly increased, polymorphonuclear cells predominating in a suppurative meningitis, lymphocytes in the non-suppurative tuberculous form. The protein content is raised and a coagulum may form in the fluid on standing. The glucose level falls and sugar may disappear, while the chloride content undergoes diminution. Finally, the organism concerned may be found. On lumbar puncture the fluid usually escapes under pressure. Excess of cells may render the fluid opalescent, while in suppurative meningitis it becomes purulent.

Symptoms.—The essential clinical features of acute meningitis are remarkably constant, though variable in intensity from case to case. They consist of intense headache, pain in the back, with rigidity of the spine. There is a characteristic combination of irritability with drowsiness, passing on to terminal coma. The patient lies on his side in an attitude of flexion and in a stuporous condition, becoming irritable and refractory when disturbed. There may be accesses of restlessness requiring restraint and periodical inarticulate cries. Retention of urine is a common and sometimes a very early phenomenon, and should always be looked for. Examination may fail to reveal any appreciable alterations in the reflexes or in the motor system, and focal signs of this order may be absent throughout the course of the case. This is especially so in acute and rapidly fatal infections.

In meningococcal and tuberculous meningitis, where the duration of the illness may be longer, cranial nerve palsies (squint, pupillary anomalies), papillœdema, variations in the tendon reflexes and signs of hemiparesis may develop, but are not essential components of the meningeal reaction. In tuberculous meningitis the knee and ankle jerks may become sluggish and disappear, sometimes relatively early in the course of the illness.

One or both of the following phenomena are usually present: *Kernig's sign*, which consists in a reflex spasm of the ham-strings when the leg is passively flexed at the hip with the knee extended, and *Brudzinski's sign*, which is a sudden flexion of the arms and legs when the head is passively flexed. It would be wrong to suppose that these signs are in themselves conclusive. They must be considered in connection with the body of clinical evidence in any given instance.

Pneumococcal Meningitis commonly complicates a pneumococcal infection elsewhere in the body, but may be primary in the subarachnoid space. The cerebrospinal fluid is purulent, and may be too thick to flow through a lumbar puncture needle. It contains an abundance of polymorphonuclear leucocytes and the organism is also found. The condition develops rapidly and coma soon supervenes.

Pyogenic Meningitis.—The streptococcus and the staphylococcus are the organisms most commonly present, and usually reach the subarachnoid space from septic foci elsewhere. The state of the cerebrospinal fluid resembles that found in pneumococcal meningitis, staphylococci or streptococci being found in abundance. The presence and nature of the primary infective focus in cranial sinuses, middle ear, or elsewhere, indicate the origin and character of the meningeal infection.

Meningococcal Meningitis (Cerebrospinal Fever) is described on page 52.

Syphilitic Meningitis is dealt with under the heading of Neurosyphilis (*vide* p. 634).

Treatment.—The relief of pain calls for the use of such drugs as phenazone or aspirin, but morphia may be required. Until the recent introduction of chemotherapy with drugs of the sulphonamide group and with penicillin, acute meningitis was, except in the meningococcal variety, virtually always rapidly fatal. Now many, though not all, lives are saved by early administration of one or both of these groups of substances. The scheme of treatment described in the case of cerebrospinal fever should be followed in other varieties of suppurative meningitis (*vide* p. 56).

Symptomatic treatment only is available in the case of tuberculous meningitis, *e.g.*, the relief of headache by drugs (aspirin with or without

¼ to 1 gr. codeine with each dose of aspirin) or by thecal drainage by lumbar puncture. The time has not come for a final assessment of the value of streptomycin.

Diagnosis.—The recognition of the presence and nature of an acute meningitis may be one of the most difficult of all diagnostic problems, because several acute general infections may be accompanied by symptoms like those of meningitis ("meningism") as an incident in their course. This is the case in typhoid, pneumonia, acute tuberculosis, and also in acute poliomyelitis. In these circumstances lumbar puncture and examination of the cerebrospinal fluid is called for to provide the necessary diagnostic information. It was taught by Jenner that whereas in a true meningitis headache and delirium may coexist, in the meningism of other infections headache disappears if delirium ensues. In true suppurative meningitis a turbid or purulent fluid containing large numbers of polymorphonuclear cells and the responsible organism will be found. In tuberculous meningitis the important features are a clear fluid, in which on standing a coagulum forms, a pure lymphocytosis, and a low chloride content (under 650 mg. per 100 c.c.), while the demonstration of tubercle bacilli in the coagulum makes the diagnosis certain. In acute poliomyelitis a clear fluid with a lymphocytosis and normal glucose and chloride contents is common, although polymorphonuclear cells are often present. In meningism the fluid is normal.

Finally, the signs and symptoms of the primary infection, both in cases of meningitis and in those of acute infections with meningism, will help to a correct diagnosis.

Hydrocephalus

Any pathological process that interferes with the absorption of the cerebrospinal fluid will cause it to accumulate within the ventricles and to distend them. In infants this distension leads to separation of the cranial bones at their sutures and to enlargement of the skull.

Such an interference with the return of the cerebrospinal fluid to the venous system may arise in any of the following circumstances: in the case of congenital anomalies of the ventricular system such as atresia of the aqueduct of Sylvius (cerebral aqueduct), or absence of the foramina of Majendie and Luschka (median and lateral apertures of the fourth ventricle); the blocking of the latter foramina by some pathological lesion; or any block in the subarachnoid space which prevents the fluid from reaching the channels of absorption above the tentorium.

Cases of internal hydrocephalus have been divided into congenital and acquired. The former are due either to such a congenital anomaly as has been mentioned or to an intrauterine meningitis with formation of adhesions. There is reason to suppose that both processes occur.

Acquired internal hydrocephalus results either from a meningitis in which the formation of adhesions has blocked the foramina in the fourth ventricle, the basal cisterns, or the opening in the tentorium. Cerebral tumours are another cause of internal hydrocephalus when they are so placed within the skull or brain that they block the ventricular outlet either at the foramina of Monro (interventricular foramen) in the lateral ventricles, at the aqueduct in the midbrain, or at the foramina of the fourth ventricle.

Most cases of hydrocephalus, if we include patients of all ages, are due to

meningitis. Even during the brief course of tuberculous and pneumococcal meningitis, signs of acute hydrocephalus may develop.

Morbid Anatomy.—In congenital hydrocephalus evidence of congenital anomaly or of meningitis may be found, but in most instances a routine examination of the brain gives no information as to cause. The development of the cerebral hemispheres is always grossly defective, and their walls may be reduced to a membrane which is translucent. The skull is increased in size, and may measure over 30 in. in circumference at birth, and the cranial vault may be reduced to the thinness of paper. The form of the skull is also altered, the frontal eminences bulging and the orbital plate being depressed.

In acquired internal hydrocephalus the rigidity of the skull prevents the extreme degree of ventricular distension and skull enlargement seen in the congenital variety. Examination of the brain generally reveals the causative lesion, either an old meningitis or a tumour.

Symptoms.—The extreme size of the skull in congenital hydrocephalus may render the delivery of the living child impossible, but such a child once successfully delivered may show progressive enlargement of the skull. In extreme cases it may be possible to transilluminate the skull, which is thin and soft. Mental and physical impairment of all degrees, from complete idiocy and physical disability to mild mental defect and little or no physical defect, may be seen. Either mental defect or symptoms of spastic paralysis may exist alone.

In acquired hydrocephalus symptoms of disordered function of the nervous system predominate, changes in the form of the skull being absent or moderate in degree. These symptoms are those of increased intracranial tension : headache, vomiting, impairment of vision, and convulsions. The long-continued distension of the ventricles produces motor and sensory disorders due to cerebral compression, motor disorders predominating. These are of the nature of a bilateral spastic weakness with the corresponding alterations in the reflexes. Percussion of the skull in children with hydrocephalus resulting from intracranial tumour may yield a " cracked pot " note. When tumour underlies the condition, death inevitably ensues.

In certain congenital and acquired (meningitic) cases the process is not progressive, and when arrest occurs before the onset of serious mental or physical disability the individual may lead a comparatively normal life.

Treatment.—Surgical procedures and repeated lumbar puncture have so far proved fruitless in all varieties of internal hydrocephalus. From what has been said of the pathogenesis of the condition it follows that purely symptomatic measures are all that are available, namely, the relief of headache and the control of convulsions, and such physiotherapeutic measures as may alleviate the motor disabilities.

THE LOCALISING SIGNS OF DISEASE OF THE BRAIN

The various ways in which a lesion may disturb the functions of the nervous system have been enumerated and described, and it follows from what was said on this subject that the nature as well as the localisation of the pathological processes may be expected to play a part in determining the character of the symptom-complex. Actually in those chronic and slowly progressive lesions which underlie the bulk of affections of the nervous

system the situation of the lesion is the determining factor in the production of the symptoms. However, in certain acute diseases and injuries of the brain, irritative and shock symptoms may appear, and their nature is largely determined by that of the pathological process, but apart from special circumstances of this kind, paralytic symptoms dependent upon the situation of the lesion are the rule. The following details may be given of the localising signs of disease of the brain :—

In general, we may say that the more rapid the development of a focal lesion the greater the disturbance of function to which it gives rise. Conversely, a slowly developing lesion may be completely masked for a long period by the development of functional compensatory activities in undamaged regions of the brain. Thus a gunshot wound of the cerebellum produces immediately a gross disturbance of cerebellar functions, while a slowly growing tumour in this situation may reach a considerable size before unequivocal signs of cerebellar disease develop.

The Signs of Local Lesions in the Cerebral Hemispheres

Lesions involving those cortical areas which stand in close functional relationship with the projection fibre systems—motor, sensory, and visual—give rise to recognisable localising signs. There are, however, large cortical association areas which are silent in the sense that disease within them produces no focal symptoms, yet in the presence of general indications of a brain lesion this absence of focal symptoms may itself be of localising value as indicating the involvement of a " silent area " of the hemisphere.

The Frontal Lobes.—Lesions at the frontal poles are frequently very difficult of recognition. The characteristic localising symptoms are mental and emotional changes. The patient becomes silent, apathetic, and lacking in initiative. Memory, judgment, and association of ideas are poor, and as a direct result of this mental state the subject becomes indifferent to the calls of nature and passes urine and fæces wherever he may be. With extensive lesions, dementia and a condition of stupor may develop. Rarely, when there is pressure upon the olfactory bulb, there are anosmia and a feeling of irritation in the nose which leads the patient to rub his nose constantly. In certain instances the patient becomes talkative and embarrassingly facetious, and holds grandiose ideas.

The Motor Area.—The excitable motor cortex occupies the ascending frontal convolution (precentral gyrus) and the hinder ends of the frontal convolutions immediately anterior. Topographically, the movements of the foot are predominantly represented at the upper end of the motor cortex ; those of the leg, trunk, upper limb, hand, neck, face, lips, and tongue in that order as we follow the convolution laterally to its lower extremity (Fig. 25). Focal or Jacksonian fits commonly begin in one of three foci—the angle of the mouth, in the thumb and index finger, or in the hallux, according to the region of the motor cortex stimulated by the lesion. Such a fit begins as a clonic, or when severe as a tonic, convulsion in one or other of these three foci. It may remain confined to this focus, or the convulsion may spread to adjacent parts and may finally involve all the musculature of one side, or become generalised throughout the skeletal musculature. In the latter case, consciousness is lost, but in localised convulsions perfect consciousness may be retained.

The spread of a Jacksonian fit shows an ordered march from its focus in accordance with the topographical representation of movements in the motor cortex. A transient paralysis of the convulsed part usually follows the fit.

One form of Jacksonian fit arising in this region of the cortex consists in transient powerlessness of a limb or part of a limb without convulsive movement. This may occur in one limb while another is convulsed.

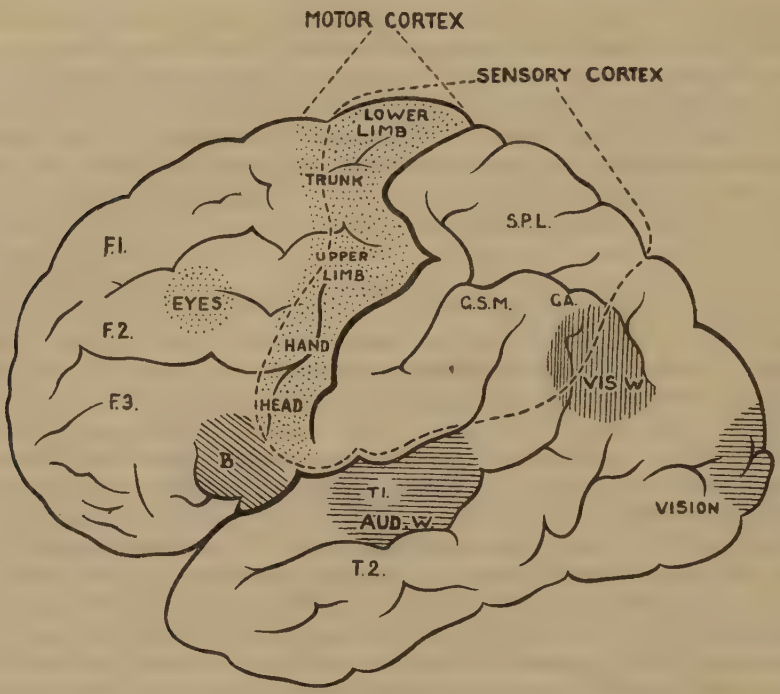

FIG. 25

CORTICAL LOCALISATION

The lateral aspect of the left hemisphere. *The motor area* extends over the ascending frontal convolution (precentral gyrus) and the cortical region immediately anterior to it. At the posterior end of the second frontal convolution (middle frontal gyrus) is a region in which eye movements are represented. Both this and the motor cortex proper are indicated by stippling. *The sensory cortex* is more extensive and includes the ascending parietal (postcentral gyrus), superior parietal, and angular (inferior parietal) convolutions (after H. Head). At the foot of, and anterior to, the ascending frontal convolution, is the so-called motor speech centre, Broca's convolution (B). In the first temporal convolution of the left hemisphere is the auditory word centre (Aud. W.), and in the angular gyrus the visual word centre (Vis. W.). The visual cortex just extends on to the lateral aspect of the hemisphere at the occipital pole.

Although movements of the eyes are not represented in the motor cortex proper but in a cortical region lying anterior to it, irritative lesions of the motor region may produce in association with rotation of the head a conjugate deviation of the eyes away from the side of the lesion. Lesions extending deeply into the substance of the hemisphere in this region may cause hemiplegia with marked spasticity.

The Sensory Area.—This has its focus in the postcentral convolution, but embraces the surrounding cortex anteriorly, posteriorly, and laterally. The essential features of sensory change from a cortical lesion are : (i) the relative integrity of sensibility to pain and temperature but a diminished power of differentiating various intensities of stimulus ; (ii) impairment of localisation of tactile stimuli, a greater degree of defect in the discrimination of two simultaneous contacts ; and (iii) a still greater impairment of the power of recognising the shape, size, and texture of objects held in the hand. With this last defect goes an inability to identify objects held in the hand ("astereognosis"). There is, in short, a defect in spatial recognition, and this is liable to lead to disturbances in co-ordination in the affected hand and digits. It is possible that Jacksonian fits which are preceded by subjective sensations in the affected part originate in this area of the cortex.

The Occipital Lobe.—The visual function is represented in the cortex surrounding the calcarine fissure (postcalcarine sulcus) on the medial aspect of the occipital lobe (*vide* Fig. 25). The right half of each visual field is represented in the left occipital cortex, the left halves in the right cortex. Further, central vision is represented at the tip of the occipital pole, peripheral vision at the anterior end of the visual area, the upper part of the field below the calcarine fissure, and the lower part above it. Irritative lesions of the visual cortex produce a visual aura in which the subject sees formless and moving coloured lights, often accompanied or followed by a transitory hemianopia. Destructive lesions of one occipital cortex will produce blindness of the crossed halves of each visual field (homonymous hemianopia), while partial lesions of one cortex may produce quadrantic hemianopia. It is characteristic of the blind retinal quadrants in occipital lesions that when a point of light is thrown upon them the pupil reacts, whereas in hemianopia resulting from lesions of one optic tract the pupil does not react on illumination of the blind part (Wernicke's hemianopic pupil reaction).

Temporal Lobe.—Perhaps the commonest localising sign in tumours of this region is a crossed homonymous hemianopia, due to involvement of the fibres of the optic radiation which curve round the inferior horn of the lateral ventricle on their way to the occipital cortex. The upper quadrant of the affected field is encroached upon before the lower. Also in lesions of the left temporal lobe slight paresis of the crossed lower face may occur, associated with a defect of the speech function of the kind known as word deafness (*vide* p. 607). Irritative lesions cause a Jacksonian fit (uncinate fit) in which olfactory and gustatory hallucinations are associated with a transient dimming of consciousness known as a "dreamy state." Sometimes, also, visual hallucinations of a complex order occur.

Internal Capsule, Thalamus, and Corpus Striatum.—Hemiplegia is the characteristic expression of involvement of the anterior limb of the internal capsule ; hemianæsthesia and hemianopia of involvement of the posterior limb. The hemianæsthesia involves all forms of sensation. Lesions in this situation may also encroach upon the lateral nucleus of the thalamus. When the latter is predominantly affected the hemiplegia tends to be transient, sensory symptoms and involuntary movements of the affected limbs persisting. All forms of sensation over the opposite half of the body may be affected, but in the case of partial lesions the sense of position is the most profoundly affected form of sensibility. In certain cases the "thalamic syndrome" may be present. In this, in addition to sensory loss there is

spontaneous pain on the affected side of the body, with a peculiar over-reaction to painful or unpleasant sensory stimuli.

The Brain Stem.—This part of the brain, from midbrain to medulla, contains structures of three orders: (i) *long projection paths*, sensory and motor, both of which are crossed—that is, have undergone decussation and run on the side of the brain opposite to that of the body which they innervate; (ii) *cranial nerve nuclei* which are uncrossed; and (iii) *association nuclei and reflex centres* which lie in the dorsal or tegmental part of the brain stem. Lesions of the brain stem may give rise to symptoms due to lesions of all or any of these three groups of nervous mechanisms. A characteristic feature of focal brain-stem lesions is a crossed hemiplegia or hemianæsthesia, with a cranial nerve palsy (of lower motor neurone type) on the same side as the lesion. Thus as we pass down the brain stem the motor cranial nerves successively involved on the side of the lesion will be the third, sixth, seventh, and twelfth. The particular nerve involved will indicate whether the lesion be in the midbrain, pons, or medulla. A lesion in the crus cerebri will produce a homolateral third nerve palsy and a crossed hemiplegia; a lesion in the ventral region of the pons, a homolateral facial palsy, and a crossed hemiplegia. Similarly, cranial nerve palsies may be associated with crossed hemianæsthesia. Lesions in the dorsal or tegmental portions of midbrain or pons will produce defects of vertical and lateral movement of both eyes respectively. Lesions in the midbrain involving the third nerve and red nucleus and superior cerebellar peduncle will produce a corresponding squint and diplopia, with involuntary movements and ataxy of the opposite side. Focal lesions in the medulla commonly prove rapidly fatal.

Cerebellum.—Gross inco-ordination of voluntary movement without considerable weakness or qualitative alterations in the reflexes are typical of lesions of this part of the brain. In acutely produced lesions there is also marked flaccidity (atonia) of the musculature, but this is apparently not a constant feature of the symptom-complex known as cerebellar ataxy. The form assumed by this ataxy naturally varies with the particular clinical test employed to demonstrate it. Thus a variety of so-called components of cerebellar ataxy have been described which for the most part have no independent existence apart from these empirical tests. The best known are as follows: *Atonia*, a marked flaccidity and undue extensibility of the muscles as revealed by manipulation of the limbs. This, when unilateral, may be an early and valuable localising sign in cerebellar abscess at a time when ataxy of movement is slight or inappreciable. *Nystagmus*, with a slow, coarse movement on looking to the side of the lesion, and a rapid, finer movement on looking away from the side of the lesion. This abnormality of ocular movement is often associated with a difficulty in conjugate deviation of the eyes, more marked towards the side of the lesion. *Adiadochokinesis*, or an inability to perform rapidly alternating (*e.g.*, pronation-supination) movements, when the single movement can be normally performed. The disability here arises from a spread of innervation to muscles which do not normally enter into the selected movement, and also from what is known as "dysmetria," which is a tendency to overshoot the mark in carrying out some co-ordinated movement. This defect may be demonstrated in various ways. Another sign of diagnostic value may be elicited by asking the patient to extend both arms rigidly before him. If both limbs be then briskly tapped, or pushed, either downwards or laterally, the limb on the affected side will be seen to

bounce or sway before coming to rest, the normal limb rapidly coming to rest. *Asynergia*, or a defective combination of the various components of a complex movement, for example, when the patient throws back his head he does not at the same time incline the trunk forwards so as to maintain his balance, and thus is apt to fall backwards. The *gait* is disordered in virtue of the defects of muscular movement we have already considered, taking on a reeling character, with a tendency to deviate towards the side of the lesion. In unilateral cerebellar lesions the symptoms described are homolateral. Speech is also commonly affected, articulation taking on a staccato, spaced quality which renders it slow and laboured. Thus the syllables of a polysyllabic word are pronounced separately as though each were a distinct word and are not normally fused into the single word.

The Corpus Callosum.—An endothelioma arising at the anterior end of the falx or a glioma in the frontal lobe may compress and distort or invade the corpus callosum. The clinical picture arising in these circumstances includes a characteristic apathy on the part of the patient, who lies motionless in bed displaying no initiative whatever, and speaking only when directly questioned. Full consciousness is retained. Urine and fæces may be passed in the bed, and there may be an associated apraxia (*vide* p. 607).

Region of Third Ventricle (*Third Ventricle, Pineal Body, and Corpora Quadrigemina*).—The common lesion in these situations is tumour. It produces internal hydrocephalus (*vide* p. 573) constantly. Compression of the superior corpora quadrigemina and the underlying nuclei of the third nerves cause loss of upward movement of the eyes and disorders of pupillary reaction. In a few cases of pineal tumour occurring in children, sexual precocity is seen. Lesions involving the floor of the third ventricle and the infundibulum also give rise to drowsiness, obesity, and polyuria (diabetes insipidus).

The Chiasmal Region.—It is commonly pituitary tumours which are responsible for lesions in this situation. These produce symptoms in virtue of (i) the disorders of pituitary function with which they may be associated; (ii) the compression and deformation of the optic chiasma they produce; and (iii) increased intracranial tension. These phenomena are considered under the heading of Intracranial Tumour (*vide* p. 580).

INTRACRANIAL TUMOURS

For clinical purposes we may include under this heading all tumours that, encroaching upon the cranial cavity and increasing its contents, produce disorders of brain function either by compression or destruction of the brain, or by both combined. Such tumours may arise in bone, in the meninges, or within the brain substance. They may be of the nature of true neoplasms or they may be granulomata. Of the former class some are primary within the skull while others are metastatic, the primary growth being situated elsewhere in the body. The brain is one of the commoner seats of tumour formation in the body.

Ætiology.—Nothing certain is known of the genesis of tumours of the brain or its coverings, although microscopic examination will suffice to tell from what element a tumour has arisen. Here, as in other organic diseases of the nervous system, injury has been invoked as an adequate exciting cause of tumour formation. It is manifestly difficult to establish a relation

between head injury and the subsequent appearance of a tumour, but on the whole it seems possible that in a few instances such an injury may excite the tissues to neoplastic activity.

Pathology.—(1) Glioma is the commonest variety of brain tumour, constituting about 40 per cent. of all such tumours. Under this heading are included all growths which arise in glial elements. These differ greatly in macroscopic and in microscopic appearance and in their rate of growth. The more the constituent cells of such a tumour differ from normal glial cells in appearance, the more malignant in character is the growth. All are infiltrating tumours arising within the brain substance. Among the types which have been differentiated the following are the most commonly encountered: (i) *Glioblastoma*, a richly cellular, rapidly growing tumour leading to death within a few months; (ii) *Medulloblastoma*, a rapidly growing, metastasising, cellular glioma, commonly growing in the cerebellum in childhood; (iii) *Astrocytoma*, a diffuse infiltrating tumour which, since its margins are not visible to the naked eye, is always very much more extensive than macroscopic examination suggests. Often only the central degenerated portions of the tumour are readily visible.

Though commonly thought to be single tumours all forms of glioma may be multiple, or may have several foci of active growth within the main tumour limits. No variety of glioma can be completely extirpated by the surgeon, and recurrence is the rule sooner or later. An exception may be made in the case of the cerebellar astrocytoma.

(2) Meningioma.—This is also a common variety of intracranial growth. It arises in cells of arachnoid origin which lie in the meshes of the dura mater. It forms a firm, well-defined mass, rounded or nodular, and exerts its effects wholly by compression of the brain, which it does not invade or infiltrate. Although it usually grows inwards towards the subjacent brain it may also develop outwards, when it invades the skull, and may give rise to a superficial "boss" on the cranial vault which is visible from without. Common situations for the development of a meningioma are the falx cerebri and the neighbourhood of the dural sinuses. It is usually a slowly growing tumour, and may give rise to focal symptoms before those indicating a general rise of intracranial tension.

(3) Pituitary Tumour.—Adenoma of the glandular portion (pars anterior) and tumour arising in the pituitary stalk (infundibulum) are the common varieties of new growth. Symptoms of three orders may follow their development: neighbourhood symptoms, signs of increased intracranial tension, and signs of glandular disorder.

Neighbourhood Symptoms.—The posterior border of the optic chiasma lies on the diaphragma sellæ and is compressed by tumours in or above the sella. The resulting symptoms are bitemporal hemianopia and primary optic atrophy, one eye being usually affected before its fellow (*vide* Fig. 27, p. 657).

Increased Intracranial Tension.—This rarely develops except in the case of pituitary stalk tumours, when headache, vomiting, and papillœdema are common, especially in childhood or adolescence.

Glandular Symptoms.—The common adenoma (chromophobe adenoma) produces signs of hypopituitarism, obesity, regression of the sexual organs with amenorrhœa in women, and loss of sexual capacity in men. In the less common chromophile adenoma, an initial acromegaly or gigantism appears,

and later obesity and other signs of diminished pituitary activity may supervene. In stalk tumours all pituitary functions are impaired. In children the Fröhlich syndrome (dystrophia adiposo-genitalis) is seen.

(4) Auditory Nerve Tumour.—A benign encapsuled tumour may develop from the sheath of the eighth nerve, either as a solitary growth or as part of a generalised neurofibromatosis (von Recklinghausen's disease). It is a fibroblastic tumour. It compresses successively the auditory, trigeminal and facial nerves, the cerebellum and pons, and ultimately gives rise to hydrocephalus and increased intracranial tension, with deafness and tinnitus, headache, vomiting, and papillœdema. Its symptomatology and the sequence of events in its evolution are indicated by the above list of structures involved.

(5) Metastatic Tumour.—This is commonly carcinoma, secondary to primary growth in lung, breast, stomach, or prostate. Rarely, hypernephroma may be followed by secondary deposits in the brain.

Secondary carcinoma commonly gives rise to multiple nodules scattered throughout the brain, and also in some instances to a diffuse microscopic infiltration of the pia arachnoid. It is the latter which gives to the clinical picture of secondary carcinoma of the brain the characteristics it usually shows: namely, an onset with mental symptoms (apathy, muttering delirium, and terminal coma), signs indicative of meningitis (pain and stiffness in the neck, cranial nerve palsies, convulsive seizures), and signs of tumour (papillœdema, headache, and vomiting). There may also be progressive loss of weight.

(6) Tuberculoma.—More common in children than in adults, this lesion may occur in any part of the brain, but most frequently in cerebellum or brain stem. It is a rounded tumour, caseous at the centre, and marked off from surrounding tissue by a zone of hyperæmia. Operative attempts at the extirpation of tuberculoma are almost invariably followed by tuberculous meningitis.

(7) Syphiloma.—Gumma is a very rare tumour. It is important to remember that a positive Wassermann reaction in the serum of a subject presenting the signs of cerebral tumour by no means indicates that the tumour is of this nature, or that anti-syphilitic medication is an adequate method of treatment.

(8) Blood-vessel Tumours.—Rarely, venous or arterial angioma may occur on the surface of the cerebral hemisphere, and are sometimes associated with cutaneous nævi in the distribution of the homolateral fifth nerve. An angioma gives rise to Jacksonian fits, and when arterial to a cranial bruit and the signs of tumour.

Hæmangioma of the cerebellum also occurs and produces the signs of a tumour in this situation.

Symptoms.—These are of three orders: *focal symptoms* due to disturbance of function in the brain region immediately involved, *general symptoms* which result from the general compression of the intracranial contents, and *epileptiform fits*, which cannot readily be placed in the first two categories, and which will be referred to later.

In many cases the general symptoms of raised intracranial tension are the earliest to appear, focal symptoms appearing relatively late, sometimes indeed as terminal phenomena. On the other hand, the signs of a slowly progressive local lesion may antedate the appearance of general symptoms of increased intracranial pressure.

Both focal and general symptoms are for the most part due to compression rather than to destruction of brain tissue. As the cranial contents increase in bulk with the development of the tumour, first the cerebrospinal fluid and then blood are expressed from the skull. When the latter occurs, cerebral functions begin to fail. The so-called localising signs are the expression of such an interference with the blood supply of the region of the brain immediately involved by the tumour. Thus the Jacksonian fits which may accompany the development of a tumour in the region of the cerebral motor cortex are in this way produced, since at a certain level of oxygen starvation the motor cells become hyperexcitable and discharge with the production of a focal convulsion.

General Symptoms.—These are headache, sickness, failure of vision, and a slowly developing blunting of mental acuity leading ultimately to stupor and coma. Not one of these symptoms is constant, at least in the initial stages of the illness. *Headache* is perhaps the most constant, though not necessarily the earliest symptom. It is often complained of as most severe on waking from sleep and after physical exertion. It may occur in paroxysms of great intensity. Its situation has no certain localising value.

Vomiting.—This is most frequent in cases with severe headache and other signs of great increase of intracranial tension. It is usual to speak of so-called cerebral vomiting as not associated with preceding nausea and as projectile in character. These characters are by no means invariable, and the undue stress laid upon them has frequently led to a failure to recognise the significance of vomiting in the early stages of cerebral tumour.

Failure of Vision is due to what is spoken of as papillœdema—that is, an œdema of the optic-nerve head. As this develops, the edges of the discs lose their definition and become hazy, the disc becomes hyperæmic and reddish in colour. The physiological pit is obliterated and the lamina cribrosa disappears from view. The veins become distended and dark in colour. Gradually the whole disc and the immediately surrounding retina rise into a hemispherical mound in which the emerging vessels are buried, and on the surface of which white exudate and hæmorrhages make their appearance. Finally, the condition of " choked disc " is reached, and vision fails rapidly and may be lost. A secondary atrophy of the nerve fibres ultimately ensues, the disc shrinks again and becomes a white opaque object, with the traversing vessels entangled in organising exudate. The retina between the disc and the macula may become œdematous during the height of the neuritis and be thrown into tiny folds, spotted with exudate at their summits, and radiating from the macula to the disc in a fan-shaped manner.

The failure of vision may be gradual, proceeding by an increasing peripheral constriction of the visual field, or it may be of dramatic suddenness. Once blindness has ensued, the pupils tend to dilate and to become immobile.

An inconstant indication of raised intracranial tension is a slowing of the pulse, which may fall below 60 per minute. This is more commonly seen, however, in the presence of subdural hæmatoma or cerebral abscess than with tumour. As a terminal sign, periodic breathing may make its appearance.

Fits.—Generalised epileptiform fits indistinguishable from those of idiopathic epilepsy not infrequently occur during the clinical course of tumour of the brain. Such fits generally indicate the cerebral hemispheres as the site of the tumour, but have no more precise localising value. Their clinical

importance lies in the fact that they may precede all other signs and symptoms, and may occur as the sole symptom over a period extending to several years. The onset of single fits, or of status epilepticus in a middle-aged person who appears in other respects to be in normal health and has been previously free from attacks of the kind should always give rise to a suspicion of cerebral tumour.

All the symptoms so far considered vary greatly in intensity from case to case. Any one or more may be absent and, as we have seen, all may fail except as terminal phenomena. They tend to be most intense in rapidly growing tumours and in tumours situated in the posterior fossa of the skull. On the other hand, they are minimal in very slowly growing tumours and in aged persons. Cerebral tumours are commonest in relatively young and middle-aged adults, and it is important to remember that the clinical combination of headache and vomiting which may precede any loss of vision (though not the optic neuritis which ultimately produces this) may be observed in individuals whose general state of health appears good and who do not seem seriously ill. As a result there is frequently a failure to appreciate the possibly sinister significance of this symptom-complex, with a resulting neglect to examine the fundi of the eyes, and an unnecessary delay in reaching a diagnosis.

Focal Symptoms.—The character of these has been dealt with in an earlier section. It has been pointed out that they may precede the signs of a general rise of intracranial tension, particularly in the case of slow-growing tumours, and it may be said that the earlier they appear, the greater their localising value. Late in the course of intracranial tumour, when there are signs of a severe degree of general compression, focal signs may appear which have no localising value whatever, and may mislead the observer who does not take the time factor into account.

In those cases in which a dangerous degree of cerebral compression develops in the absence of equivocal focal symptoms, mention may be made of a unilateral diminution or disappearance of the abdominal reflexes as indicative of a tumour of the opposite side of the brain.

The Cerebrospinal Fluid.—On lumbar puncture the fluid may be found to be under considerable pressure (300 to 1,000 mm. water), but otherwise normal except in those cases where the tumour comes in contact with the fluid, either in the ventricles or at the base of the brain. In these circumstances a protein increase may be found.

Age Incidence.—A word is necessary on this subject. Not only have the different histological varieties of tumour their favourite sites of incidence in the brain, but also characteristics of age incidence.

During the first ten years of life, medulloblastoma in the fourth ventricle is the common tumour. Its clinical picture includes the signs and symptoms of raised intracranial tension, unsteadiness of gait, and bilateral external rectus palsy.

In the second decade, pituitary stalk tumours frequently reveal their presence. In adolescents, this tumour often produces the signs of raised intracranial tension, papillœdema, headache and vomiting, together with signs of hypopituitarism, but in adults primary optic atrophy and bitemporal hemianopia are the rule.

Astrocytoma occurs at all periods of life—in the cerebellum in childhood, and there and in the cerebral hemispheres in adult life.

Meningioma, glioblastoma, and auditory nerve tumour occur in the middle and later periods of life.

Diagnosis.—The recognition of an intracranial tumour is, perhaps, most difficult in those cases where focal symptoms are present and there is no evidence of compression of the cranial contents as a whole—that is, no papilloedema, headache, or vomiting. In such a case the organic origin of the focal signs having been determined on the grounds detailed in the introductory chapter to this section, it remains to ascertain whether a tumour is responsible for their appearance. The feature of most importance in this connection is a progressive development of the signs and indications of successive involvement of more functions (*i.e.*, of expansion of the lesion). Thus, while a sudden onset of hemiplegia probably indicates a vascular lesion of the brain, a slowly developing hemiplegia, especially if its progress be punctuated by focal or Jacksonian fits, is almost certainly due to tumour.

In respect of the general symptoms, especially where these exist without focal signs, we have to assess the significance of papilloedema, headache, and vomiting. The combination of vomiting and headache, with or without giddiness, especially in a subject who presents no clear indications of a gastric lesion or arteriosclerosis, should always lead the observer to suspect cerebral tumour and to examine the optic discs. Papilloedema may be present for a considerable time before there is any appreciable failure of vision, and thus may have to be looked for. The diagnosis of tumour may present considerable difficulties when there is no other objective sign than papilloedema. The high degree of swelling of the discs associated with tumour is not seen in other conditions, but the lesser degrees of swelling and the associated hæmorrhage and exudate may closely resemble the neuroretinopathy of malignant hypertension (*vide* p. 430). The symptoms associated with this condition, headache, vomiting, and convulsions, may suggest a cerebral tumour. Therefore, in the absence of focal paralytic signs, the possibility of malignant hypertension must always be considered when papilloedema appears. Chronic lead poisoning may also produce a clinical picture resembling that mentioned above.

Abscess of the brain, which is in effect a fluid tumour and may be associated with considerable local œdema of the brain, may also have to be considered. The presence or absence of chronic suppuration in the cranial venous sinuses, and particularly in the middle ear, should therefore be determined. A gummatous meningitis may give rise to a clinical picture resembling that of tumour, but in this condition the swelling of the discs is rarely extreme, or the impairment of vision gross, and such paralytic phenomena as are present are not severe except in the case of the cranial nerves. Nevertheless, when the presence of a cerebral tumour is suspected, and especially if papilloedema is present, the diagnostic use of lumbar puncture is contraindicated. The removal of cerebrospinal fluid allows the cerebellum to be forced downwards into a pressure cone in the foramen magnum, this in turn induces a dangerous compression of the brain stem with its contained vital centres, and may lead to rapid and fatal respiratory failure.

When localising signs are lacking, or even when the presence of tumour is suspected but cannot be confirmed, additional information may be obtained by one or other of the applications of radiography. A simple radiogram may reveal bony changes which indicate the presence and situation of the tumour, *e.g.*, deformation of the pituitary fossa in pituitary tumours, shadows cast by

calcareous material in a slow growing tumour, lateral displacement of a calcified pineal gland, thinning of the skull, invasion of the skull by an endothelioma, or, in children, separation of the sutures.

When these fail to provide information the injection of air into the ventricles (ventriculography) may show dilatation or displacement of the ventricular system. The injection of air by lumbar puncture (encephalography) will reveal abnormalities of the cerebral sulci, and finally the injection of opaque substances (thorotrast) into the carotid artery (angiography) followed by radiography will reveal displacements of the cerebral arterial tree. Ventriculography and encephalography are not wholly free from danger, while the resulting radiograms call for skilled interpretation. They are, therefore, best undertaken by the neuro-surgeon under conditions that allow of immediate operation if any untoward reaction results. It is not necessary to describe the technique of these procedures here. Recently claims have been made that the electro-encephalogram (*vide* p. 648) may yield localising information of value when this is not otherwise obtainable, but the results of this are not yet sufficiently reliable for much stress to be laid upon it here. It may be said, however, that simple clinical examination often fails to localise a new growth within the skull and that the ventriculogram, expertly taken and interpreted, is not rarely necessary in the complete investigation of a suspected case of intracranial tumour.

It is always important not to forget that an intracranial growth may be metastatic, the lung being perhaps the commonest seat of the primary growth in these circumstances. Therefore a careful general examination of the patient and an X-ray examination of the chest are important elements in the diagnosis of intracranial tumour.

Course and Prognosis.—When allowed to run their course, intracranial tumours almost invariably cause death. From the moment when diagnosis becomes possible life is rarely prolonged for more than a year. With increasing compression of the cranial contents the patient becomes blind, and finally comatose, dying of respiratory failure. The last-named terminal phenomenon may occur suddenly from hæmorrhage into the tumour, or from some other cause of sudden rise of pressure within the skull.

Rarely, a tuberculoma will become inactive, or a glioma cease to grow, but these events are exceptional.

Treatment.—There is no cure for intracranial neoplasm other than its removal by surgical operation. When it is possible to localise the growth, the attempt at its extirpation will depend upon anatomical and pathological factors. If it be by its situation accessible, is it of a kind that can be removed ? The glioma, from its diffuse infiltrating character, clearly offers little prospect of complete removal, and the attempt may involve gross damage to brain tissue which is still functioning, and a corresponding degree of physical disability for the patient. The meningioma and neurofibroma, on the other hand, when accessible are favourable for complete or partial extirpation, and the best results have been obtained in cases of this kind.

When the tumour is inaccessible to the surgeon, irremovable from its character, or cannot be localised, palliative measures only can be adopted. These consist in the use of X-rays or of radium applications to retard the growth of the tumour. For headache, analgesic drugs may be tried ; but in extreme instances morphia may be required, and its use in adequate doses is amply justified.

CHRONIC SUBDURAL HÆMATOMA

The condition to which this name is applied has been regarded as inflammatory in origin, but it is practically certain that it is always traumatic and the result of venous oozing into the subdural space.

Ætiology.—The essential lesion appears to be the tearing of the small veins which pass from the arachnoid to the dura mater on their way to the venous sinuses which lie in the latter. Relatively trivial jarring blows on the head, not necessarily of a degree of violence productive of concussion, are most likely to produce the venous lesion in question. The veins once injured, slow and intermittent oozing leads to the gradual development of a subdural hæmatoma. A subdural hæmatoma may be the immediate result of a severe head injury which necessarily comes under observation and treatment from the outset. We are not here concerned with this type of subdural hæmatoma but only with that which follows apparently trivial injuries that receive little or no treatment and may not even come under observation. This chronic variety of hæmatoma reveals its presence after a latent period of varying length by symptoms suggestive of a progressive space-occupying lesion. It is with this that the present section deals.

Morbid Anatomy.—A collection of blood, often very large, is found situated beneath the dura over the convexity of the cerebral hemisphere and extending from the frontal to the occipital lobes, but seldom passing farther laterally than the Sylvian fissure (lateral sulcus). It is commonly bilateral, though not invariably so. The blood is encapsuled in a membrane which is loosely attached to the overlying dura, and may receive a free vascularisation from this source. The deep surface of the cyst is lightly adherent to the subjacent pia-arachnoid. On its internal surface the membrane is rough from adherent clot. The contained blood is tarry and liquid in long-standing cases, and the enclosing membrane may be discoloured by it. The state of the blood and the thickness of the cyst wall vary with the age of the lesion.

Symptoms.—The history of a fall on the front or back of the head is frequently to be obtained. This may have been apparently trivial and not followed by any immediate consequences. Prodromal symptoms appear after a varying interval of from a week to two or three months. Headache and slight mental change are the most constant of these. The headache may be constant and severe, and may be referred to the site of the injury; there may be associated vomiting. Gradually apathy, drowsiness, and forgetfulness develop, and there may be "fainting attacks." Physical examination may be negative at this period, and neuro-syphilis or some mental disorder may be diagnosed. When these symptoms have been present for some four or six weeks they may suddenly become severe. Intense headache and vomiting with sudden coma may develop, only to pass off in an hour or two, returning again after an interval of days. Focal symptoms are often absent, or when present are variable in their appearance. Evidence of bilateral compression of the cerebral hemispheres ultimately develops: hemiparesis, muscular spasticity, bilateral loss of the abdominal reflexes, Babinski plantar responses, and optic neuritis. Once these signs are established the condition grows steadily worse, and unless treated the patient lapses into coma and dies. The pulse is often slow even in the early stages of the condition.

Diagnosis.—In the presence of a history of apparently slight head injury, the premonitory period of vague and transient headaches and mental change,

the appearance of definite stupor or coma after some weeks, and the variable appearance of the signs mentioned above, together present a very characteristic clinical picture, of which the very fluctuation of the signs and symptoms is one of the most striking features. Confirmatory evidence may occasionally be obtained by lumbar puncture, the cerebrospinal fluid being sometimes faintly tinged with yellow, though normal in other respects, but as a rule the fluid is colourless. It should be remembered that this lesion may occur at any age from infancy onwards.

Treatment.—This is exclusively surgical, and when the hæmatoma is of any size death ensues unless the clot be removed. That the malady is not invariably fatal, however, is seen by the finding at post mortem of long-standing lesions of this kind in elderly and demented subjects who have succumbed to some other malady.

CEREBRAL ABSCESS

(*Suppurative Encephalitis*)

Pyogenic organisms may reach the brain by direct implantation in cases of injury to the skull and meninges, by direct spread from a local focus of suppuration, or by the blood stream from some remote focus of infection.

Traumatic Abscess, though frequent in gunshot wounds of the skull, is relatively uncommon in civil practice. Single or multiple abscesses develop in the track of the infective material.

Local Suppuration in the skull is the common cause of abscess of the brain, and more than half the total number of abscesses seen arise in association with chronic otitis media. Caries of the petrous bone is the common antecedent of infection of the brain, and a cholesteatoma is found in most cases. Occasionally frontal sinus disease may result in abscess formation in the frontal pole of the hemisphere.

In the case of otitis media, either the temporal lobe (two-thirds of the cases) or the anterior part of the cerebellar hemisphere (one-third of the cases) is infected. In the former instance the tegmen tympani is carious, and a definite track may be traceable from the middle ear through the bone and dura into the brain. Occasionally a small abscess forms between dura and brain, but as a rule no definite track exists, and there is a thin layer of intact brain on the under surface of the lobe between abscess and meninges. When infection spreads through the posterior wall of the mastoid (tympanic) antrum, the cerebellum is the seat of abscess formation.

Pyæmic Abscess.—In the majority of cases of pyæmia the brain is not infected, but there is a peculiar tendency to the formation of a single abscess in either frontal or occipital lobe in cases of chronic suppuration within the thorax (chronic empyema, bronchiectasis), and this is then usually the sole pyæmic manifestation. Surgical intervention in a case of chronic empyema is sometimes the immediate cause of abscess formation in the brain.

When the suppurative process develops very rapidly, the brain softens and becomes diffluent, suppuration reaches the ventricles or the surface, and death ensues within a few days. No definite circumscribing wall can be found to the necrotic purulent material. Clinically, a diagnosis of abscess cannot be made with a process so rapid, and symptoms of acute leptomeningitis may dominate the picture. With a more slowly developing process an

abscess cavity forms, and in from five to six weeks a definite enclosing capsule surrounds it. In long-standing cases this capsule may be extremely tough and thick, so as to allow of the abscess being removed intact. Further, such cases may run a long and latent course, the abscess suddenly bursting on to the surface of the brain or into the ventricles after a period of one or more years. This has been especially the case in abscesses forming in the track of a bullet.

Symptomatology.—As has been already mentioned, acute spreading suppuration so rapidly causes death with symptoms of an acute meningitis that a diagnosis of abscess cannot be made. In chronic cases a circumscribing capsule tends to localise the suppuration, and a well-defined abscess forms. It may give rise to three orders of symptoms : those of suppuration, those of a rise of intracranial tension, and focal signs determined by the seat of the lesion. Indications of a general septic process may be wanting, but when present consist of one or more rigors, a febrile reaction, and a leucocytosis in the blood. Pallor and progressive wasting may also occur in long-standing cases.

The symptoms of raised intracranial tension have already been dealt with under the heading of Cerebral Tumour, and here, as in the case of tumour, depend for their intensity and time of appearance upon the rate of development of the abscess. In certain chronic abscesses there may be a period of over a year in which no symptoms whatever are present. In these circumstances the bursting of the abscess into ventricles or on the surface of the brain is the first indication of abscess, and gives rise to acute and rapidly fatal symptoms : convulsions, coma, and death.

In the common case, that of otitic abscess, there is a period of from one to several weeks during which no definite symptoms are noticed. Then, headache, apathy passing into drowsiness, a subnormal temperature of about 97° F., and a slow pulse of from 60 to 40 per minute indicate the slow growth of an encapsuled abscess.

Such a sequence of events in a case of chronic otitis media, or frontal sinus disease, should early give rise to a suspicion of abscess. In the initial phases there is not often a complaint of failing vision, but examination will reveal an engorgement of the disc with haziness of its edges, or a frank papill-œdema. Vomiting may occur, but is not prominent in every case. Focal symptoms in the case of temporo-sphenoidal abscess are determined by the spread of pressure to adjacent regions of the brain. Thus pressure upwards will involve the lower end of the cerebral motor cortex and produce paresis of the lower face ; pressure mesially will affect the pyramidal system and produce hemiparesis, in which the leg may be more definitely weak than the arm or face. Occasionally signs of midbrain compression are seen : paralytic dilatation of the homolateral pupil, ptosis, and squint with diplopia. When the left temporal lobe is involved, the disturbance of the speech function known as word-deafness may be present. An isolated external lateral rectus weakness with trigeminal pain in children (*Gradenigo's syndrome*) with mastoid disease may be due to a localised meningitis over the petrous bone (petrocitis), and does not necessarily indicate abscess.

In cerebellar abscess the relatively small size of the posterior fossa of the skull tends to the early development of both general and focal symptoms. The most important of the latter are :—

1. *Nystagmus.*—This is most distinct when the eyes are turned towards the side of the lesion, and then consists of a slow ample movement to the side

of the lesion, with a quick return. On deviation to the side opposite the lesion, nystagmus may be less well defined, and tends to be a more rapid and less ample movement than when the eyes are directed towards the side of the lesion. Nystagmus is not necessarily the earliest focal symptom present.

2. *Atonia and Ataxy* of the limbs on the side of the abscess. The arm musculature is flaccid, and on movement the phenomena of cerebellar involvement described on page 578 are seen.

3. *Paralyses of Cranial Nerves*, third, fourth, fifth, sixth, seventh, and eighth may be present on the side of the lesion, but the localising value of these signs is less certain than those of cerebellar compression, since some of them may be present as a result of middle ear disease (seventh and eighth), and a sixth nerve palsy occurs with raised intracranial tension in lesions which do not directly involve the nerve.

If diagnosis be not made at a time when atonia and slight inco-ordination of the limbs, with or without definite nystagmus, are alone present, the progressive drowsiness of the patient will probably prevent adequate examination.

4. *The Cerebrospinal Fluid.*—In most cases there is a moderate increase in the cellular and protein content of the fluid. Up to 30 cells per cubic millimetre may be found, the majority being lymphocytes, and not more than 5 per cent. polymorphonuclear cells. When a subacute localised meningitis develops, the cell count rises considerably higher but often remains predominantly lymphocytic, but with an acute spreading meningitis polymorphonuclear cells predominate.

The chlorides and the glucose remain normal unless a meningitis supervenes, when a drop in the percentage of both occurs.

Diagnosis.—Cerebral abscess may have to be differentiated from tumour, sinus thrombosis, and meningitis. In the case of pyæmic abscess the differentiation may be impossible apart from the history of the case and the presence of signs of chronic suppuration in the thorax. Thus the development of signs of intracranial hypertension after operation on a chronic empyema, or in a patient with bronchiectasis, is presumptive evidence in favour of abscess. The clinical signs of an acute infection of the meninges with the appropriate changes in the cerebrospinal fluid, and rapid downward course of the case usually serve to differentiate generalised meningitis from abscess. In *lateral sinus thrombosis*, signs of general septic infection are prominent: repeated rigors, fever, embolic phenomena, and rapid wasting. Headache, restlessness, delirium, vomiting, and even papillœdema may occur though no abscess be present. This combination of symptoms, associated with a normal cerebrospinal fluid, has been spoken of as "otitic hydrocephalus" and is treated by repeated lumbar puncture. Occasionally, however, patients with lateral sinus thrombosis may show relatively few symptoms and signs.

The Treatment of cerebral abscess is exclusively surgical, and in the absence of effective drainage, death is inevitable.

CEREBRAL VASCULAR DISEASE

I. Anatomy

The frequency with which pathological changes in the arteries supplying the brain give rise to both acute and chronic disease of this organ makes a

brief statement of some of the main anatomical features of the cerebral circulation essential.

Arterial blood reaches the brain by the two internal carotid and vertebral arteries.

The Vertebral Arteries enter the skull by the foramen magnum and, meeting on the ventral surface of the brain stem, join to form *the basilar artery* at the level of the lower border of the pons. This vessel continues upwards to the level of the convergence of the crura cerebri (cerebral peduncles) as they enter the brain stem, and then divides into the two *posterior cerebral arteries*, which at once sweep lateralwards round the crura to gain the inferior surface of the temporal and occipital lobes which they supply with blood, together with the marginal zone of the lateral aspect of these lobes.

From the basilar and vertebral arteries, as they lie on the ventral surface of the brain stem, perforating and terminal branches enter the medulla, pons, and midbrain. There also arise on each side of these arteries the three cerebellar arteries : posterior inferior, anterior inferior, and superior cerebellar, which pass lateralwards and, giving off perforating terminal branches to the brain stem as they traverse its surface, end in a series of anastomosing branches on the cerebellar cortex.

The Internal Carotid Artery on each side enters the skull by the carotid canal, and passing upwards on the lateral aspect of the body of the sphenoid bone reaches the neighbourhood of the posterior clinoid process and the optic chiasma. Here, after giving off the ophthalmic artery, which enters the orbit, it divides into three terminal branches, the middle and anterior cerebral arteries and the posterior communicating artery.

The Middle Cerebral Artery turns lateralwards from its point of origin, and as it traverses the anterior perforated space (substance) gives off its perforating or central branches, which pass deep into the region of the lenticular (lentiform) nucleus, internal capsule, and thalamus. The main trunk then enters the Sylvian fossa and finally emerges on the convexity of the hemisphere at the anterior end of the Sylvian fissure (lateral sulcus) and near the foot of the fissure of Rolando (central sulcus), where it breaks up into cortical branches which supply all but the marginal zone of the lateral aspect of the hemisphere. One branch runs as far backwards as the occipital pole, where it is said to anastomose with branches of the posterior cerebral artery. *The anterior cerebral artery* runs forwards and towards the middle line dorsal to the optic nerve and, entering the great longitudinal fissure, comes to lie parallel to its fellow, to which it is joined by the anterior communicating artery. Both anterior cerebral arteries then sweep forwards round the genu of the corpus callosum, and reaching its upper surface supply branches to the medial aspect of the hemispheres and to a narrow marginal zone of the convexity in frontal and parietal regions.

Lying in the subarachnoid space at the base of the brain are the origins of the three cerebral arteries, and with the communicating arteries they make up the circle of Willis (arterial circle).

II. Ætiology and Pathology

The causation and morbid anatomy of arterial disease and the relation of this to the clinical states associated with it nowhere present more obscure

problems than in the case of the arteries of the brain. The difficulty that pathologists experience in finding those arterial occlusions by clot, and the arterial ruptures, that we have for so long supposed to underlie cerebral thrombosis and hæmorrhage respectively, imply that the accounts of these things given in textbooks of neurology have become too conventional and oversimplified. It is probable that we have taken too little account of the possible roles of vasomotor disorders in these arteries in leading to cerebral softening and hæmorrhage. On no hypothesis of arterial occlusion by clot can we account for the fugitive hemiplegias and other transient paralyses of cerebral function that we encounter in hypertensive subjects, often preceding the later development of more severe and persisting paralyses. It may be that the familiar triad, hæmorrhage, embolism, and thrombosis, should be replaced by the two main categories of hæmorrhage and softening. Subdivisions of the latter would include softening from embolism and also from vasomotor disorders (vasospasm and vasoparalysis). The hypertensive crisis and the state known as hypertensive encephalopathy may also, in part at least, be expressions of vasomotor disorder, preceding or accompanying structural lesions in cerebral arteries and arterioles. In short, we may suppose that underlying cerebral disorders from vascular disease there are three essential factors, two cerebral, one extracerebral, namely, (i) abnormal vasomotor disorder in cerebral vessels, (ii) structural disease of cerebral vessels, and (iii) fluctuations in cardiac efficiency from heart disease. Some would now add a fourth—a psychological—factor, which they regard as capable of initiating vasomotor disorders, whence structural lesions may follow. How this may happen is neither known nor suggested, but there is some evidence that it may so happen.

With at least four factors in operation, varying in their relative importance from case to case, it is not surprising that the clinical pictures of cerebral vascular disease are very numerous and diverse in form and behaviour.

This is not the place to discuss in any detail the morbid anatomy of arterial disease, but brief reference is necessary to the two main varieties found in the arteries of the brain.

Atherosclerosis (or atheroma) is the process found in the large cerebral arteries. It is a patchy and nodular process, leading to distortion of the vessel and even to narrowing or occlusion of its lumen. The intima is the seat of the essential lesion, which consists in fatty deposition, followed by sclerosing changes in the intima and some calcification. These lead to aneurysmal dilatation and even to rupture as well as to narrowing.

Arteriolosclerosis (or hyperplastic sclerosis) is a diffuse process characteristic of the intimate vasculature of organs, pre-eminently of the kidney, but found also in the brain. It is the change found in association with hypertension, and has been thought to be a response to this. A hyaline change and thickening of the subendothelial layer of the intima is the essential lesion, and it leads to narrowing and even to occlusion of the arteriolar lumen.

We see, therefore, that the larger arteries of the brain become the seat of the patchy change known as atherosclerosis, while the arterioles show a diffuse change of a different character. In some subjects of cerebral vascular disorder both varieties of arterial change may be present, while in others one or other variety may predominate.

Too little is known of the role of vasospasm in producing cerebral hæmorrhage and softening to allow of dogmatic statements, but it is possible

that when softening ensues upon atherosclerosis of the larger arteries we are dealing with occlusion of an already narrowed artery by blood clot, a true thrombosis, while the softening that ensues upon the sclerosis of arterioles may result as frequently, or even more frequently, from spasm as from clot formation. Throughout this section, therefore, the word thrombosis is used "without prejudice" as it were, and it is to be understood that in many instances of so-called cerebral thrombosis the essential factor may have been a transient arteriolar spasm, leading to an ischæmia of sufficient duration to lead to softening of cerebral tissue.

A further point remains: it is clear that if cardiac weakness supervenes in a subject with cerebral arterial disease, the addition of this further factor may lead to disaster by still further impeding the cerebral circulation. In these circumstances a failing heart may precipitate a cerebral vascular disaster, and thus it is that some cases of terminal heart failure present a strikingly cerebral symptomatology.

Rupture and Hæmorrhage in most cases occur on the lenticulo-striate branch of the middle cerebral artery, particularly on the left side, with the result that this branch has been named "the artery of cerebral hæmorrhage" by Charcot. Whether the miliary aneurysms which stud the perforating branches of the middle cerebral artery are themselves the cause of rupture is disputed, and it is thought that they may be normally present, rupturing only when their walls are damaged by degenerative changes. Another not infrequent seat of rupture is one of the perforating branches of the basilar artery in the substance of the pons.

Cerebral hæmorrhage may occur in acute leukæmia and in thrombocytopenic purpura, often as a terminal event. The diagnosis is usually obvious.

Factors tending to precipitate rupture are the cardiac hypertrophy and high blood pressure often found in those with diseased cerebral arteries. It follows from these pathological considerations that hæmorrhage is an accident of elderly persons, being rare before the age of forty and increasing in frequency with each subsequent decade. Occasionally in the young subjects of chronic nephritis with an associated high blood pressure and arterial degeneration, cerebral hæmorrhage may occur.

The effused blood, pouring from the ruptured lenticulo-striate artery, tears up the white matter of the centrum semiovale and the corpus striatum, and compresses the adjacent brain tissue. The blood may burst into the lateral ventricle or on to the surface of the hemisphere, where it spreads over the convolutions beneath the pia arachnoid. Extravasations of blood may be of considerable size, rendering the affected hemisphere larger than its fellow and producing flattening of the convolutions and local œdema of the brain surrounding the clot. In small hæmorrhages which the patient survives, the clot shrinks, and may be completely absorbed, its place being taken by scar tissue or by blood-stained fluid. At the periphery of the clot neuroglial proliferation leads to the formation of trabeculæ, which form a wall to the cavity.

On the other hand, when arterial disease leads to *occlusion and cerebral softening*, any of the main arteries of the brain or their branches may be involved, although even here the middle cerebral and its central branches are most commonly affected. The result of infarction of the brain is to produce swelling and serous effusion into the ischæmic region, which rapidly softens.

and within a few days is of creamy consistence. The softened area may be white or red, the latter when rupture of vessels at the periphery of the infarct has occurred. When the patient survives, the necrosed tissue is absorbed and its place taken by a cavity, single or multilocular, filled with clear fluid.

Hyperpiesia (Essential Hypertension) **and Hypertensive Encephalopathy.**—The condition described under these names on page 427 is not infrequently marked by the development of conspicuous but transient disorders of cerebral function. These are grouped together under the name of Hypertensive Encephalopathy.

Two forms of hypertensive attack have been described :—

1. *With Malignant Hypertension.*—This is said to occur in childhood, adolescence, or early adult life. The subject may have essential hypertension without renal lesion, or may have acute or chronic nephritis. A sudden rise in blood pressure is followed by headache, vomiting, and drowsiness. There may be convulsions, or hemiplegia, or other signs pointing to some focal brain lesion. There is retinitis, usually with marked swelling of the optic discs, hæmorrhages, and exudate on the retina. Recovery may take place in a few days, but the patient remains liable to recurrences, any one of which may terminate in fatal cerebral hæmorrhage.
2. *With Benign Hypertension.*—The patient is commonly a middle-aged or elderly subject with high blood pressure, and the attack consists in the appearance and rapid disappearance of such focal signs as hemiplegia, aphasia, hemianopia, or focal convulsion. There is no swelling of the optic discs, but hypertensive retinitis is commonly present.

In both types, when uncomplicated, there are no signs of renal inadequacy and the blood urea remains within normal limits.

In both types, also, spasm of the cerebral arteries has been invoked to explain the transience of what may be severe paralyses. Sooner or later the subjects of hypertensive encephalopathy succumb to cerebral vascular lesions.

Treatment.—When signs of cerebral œdema are noted, venesection and the administration of hypertonic saline are indicated ; 70 c.c. of the latter are given intravenously (15 per cent. sodium chloride), or the same quantity of 50 per cent. sucrose solution. When the case is less urgent, ½ oz. of magnesium sulphate in 6 oz. of water may be given per rectum and repeated as necessary.

Syphilis.—The common syphilitic lesion of cerebral arteries is endarteritis obliterans, involving the central branches of the middle cerebral arteries, and less commonly the deep perforating branches of the basilar and vertebral arteries which supply the brain stem. Arterial occlusion and softening of the affected region of the brain are the results of this lesion. Not uncommonly other syphilitic lesions of the nervous system accompany endarteritis, namely, gummatous meningitis at the base of the brain, or tabes.

Embolism.—In this condition the morbid process lies remote from the brain, somewhere between the pulmonary veins and the aorta. Possible sources of emboli are the vegetations on the mitral valve in endocarditis with mitral stenosis. More often, however, in this lesion clots may form in the

auricular appendix (auricle), and fragments may be dislodged and carried off in the blood stream. Finally, in atheroma of the aorta, tiny pieces of degenerated tissue or of thrombi may be detached and form emboli.

These emboli when they reach the cerebral circulation are commonly arrested, either in the main trunk or in one of the cortical branches of the middle cerebral artery, the left more particularly. Here they produce an infarct resembling in appearance and results the infarction of thrombotic occlusion. Occasionally the anterior and posterior cerebral and the vertebral arteries are the seat of embolic arrest, while very rarely the internal carotid may be blocked in this way. When this occurs the ophthalmic artery is also deprived of blood. It is clear that the disturbances of function produced by embolism are absolutely sudden in onset.

Aneurysm.—It is preferable to deal with aneurysms of the larger cerebral vessels separately, as they may arise from a variety of causes. The circle of Willis (arterial circle) with the trunks arising from it and the basilar artery are the usual seats of aneurysmal dilatation. In the case of the last-named vessel, syphilitic arteritis may be responsible, and the dilatation may reach such a size that the symptoms of tumour are produced. In the case of the other vessels, however, other causes than syphilis are more important. Thus it is thought that certain aneurysms on the circle of Willis may be congenital in origin, occurring at points of arterial junction and branching where the walls are thin from developmental defect. The arrest of an infective embolus may produce a local inflammation of the arterial wall with resulting sacculation. Finally, the atheromatous changes described above may produce aneurysms in these regions. In children and young adults these aneurysms are mainly congenital, but in elderly persons atheroma plays a larger role in their formation. In most instances these aneurysms do not rupture, and give rise to no symptoms during life. However, they may leak, or may burst with considerable effusion of blood and rapid death.

The blood thus effused spreads in the subarachnoid cisterns at the base of the brain, traverses the Sylvian fossa and spreads over the convexity of the hemispheres, gravitates downwards into the spinal theca where its presence may be revealed by lumbar puncture, may burst into the substance of the hemisphere, and even penetrate into the lateral, third, and fourth ventricles. Occasionally an unruptured aneurysm of the internal carotid artery gives rise to pressure symptoms. These are third nerve palsy (ptosis. dilated and immobile pupil, external squint), pain in the distribution of the second division of the fifth nerve, sometimes blindness in the eye on the affected side, and proptosis. This picture may be followed by the appearance of signs of subarachnoid hæmorrhage.

From this brief summary of the various arterial lesions in vessels supplying the brain, we may draw the following conclusions : (i) that cerebral embolism is most common in young persons, particularly women, with endocarditis and mitral stenosis, or in persons with subacute bacterial endocarditis ; (ii) that cerebral hæmorrhage is a disease of elderly persons, particularly males, with atheroma, cardiac hypertrophy, high blood pressure, and granular kidney ; (iii) that cerebral softening may occur in elderly persons of the type indicated under (ii), and also in young adults, particularly males, who are syphilitic ; (iv) aneurysms at the base of the brain are of variable ætiology, and may be found in persons of all ages, and may give rise to symptoms at any age commonly by rupturing.

III. Symptomatology

A sudden onset with a " stroke " or apoplexy is a feature common to all extensive vascular lesions of the brain, be they due to hæmorrhage, embolism, or thrombosis. When, as is commonest, the lesion involves the region supplied by the middle cerebral artery, the residual and permanent disturbance is hemiplegia. There is a close resemblance, therefore, between the initial and the residual symptoms caused by these three vascular lesions. It is often difficult to differentiate hæmorrhage from thrombosis at the time of onset,

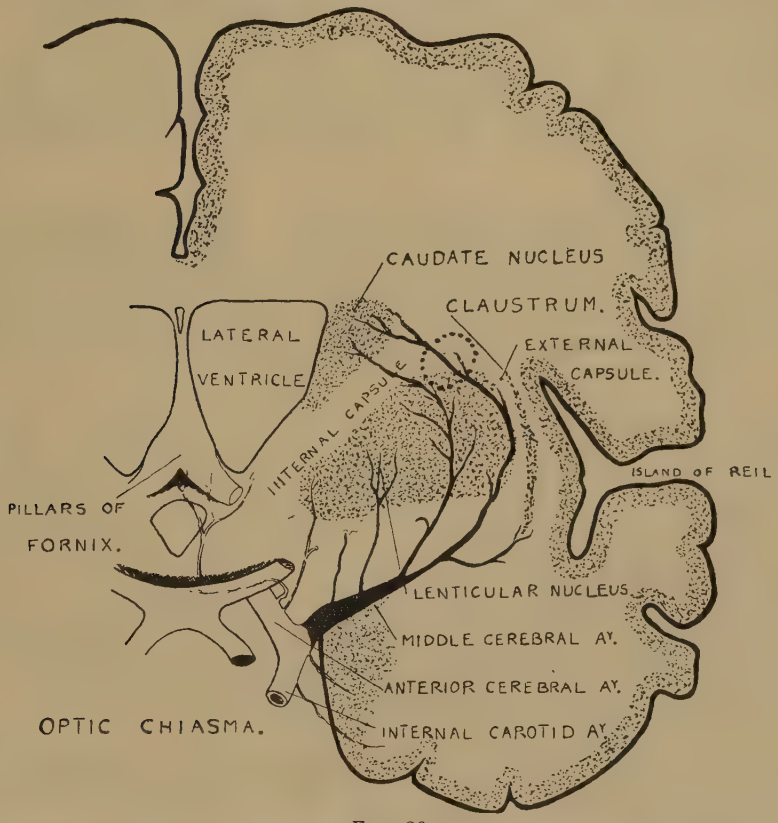

Fig. 26

Coronal section of the left cerebral hemisphere, showing the central branches of the middle cerebral artery. The region of the lenticulo-striate artery, which is commonly the seat of rupture and of cerebral hæmorrhage, is indicated by a circle of dots.

though cerebral embolism is, for reasons which will be given, commonly recognisable as such, but the hemiplegia is in each case identical in character. The features of the apoplexy due to each lesion may be separately described and a discussion of their clinical differentiation will be given later.

(*a*) **Hæmorrhage.**—In the case of intracerebral hæmorrhage the seat of rupture is usually in the region of the corpus striatum, anteriorly near the caudate nucleus, laterally in the external capsule from the lenticulo-striate artery, or posteriorly between the thalamus and the lenticular (lentiform) nucleus. In every case the blood invades the lenticular nucleus and internal capsule (Fig. 26).

Rarely premonitory symptoms are present, consisting of headache, vertigo, mental confusion, and disturbance of speech, with unilateral paræsthesiæ and weakness. These are rapidly followed by the apoplectic seizure. In severe cases the patient is deeply unconscious, the face may be flushed, or less commonly pale, the body is covered with perspiration, and the pulse is slow and hard. Respiration is laboured and stertorous. Urine and fæces may be voided, and the muscles are completely flaccid. The pupil and tendon reflexes are frequently absent. In these circumstances death may ensue within a few hours, and is preceded by Cheyne-Stokes breathing and an acceleration of the pulse. The temperature may fall one or two degrees and remain below normal until death, but when life is prolonged the initial depression gives place to a slight febrile reaction which lasts for some days. Vomiting sometimes occurs at the moment of onset, but convulsions are exceptional. Frequently, when coma is deep, blisters appear on the heels and other dependent parts.

If death does not ensue, consciousness begins slowly to return after some hours, and delirium and restlessness may appear. Death follows, in at least 30 per cent. of cases of cerebral hæmorrhage, within the first two days. While the patient is yet unconscious, signs of a unilateral lesion may be discoverable, and on return of consciousness a residual hemiplegia is revealed.

This description applies to the common case of hæmorrhage from the middle cerebral artery. In the case of certain other vessels the symptomatology may vary in detail.

Pontine Hæmorrhage.—Apoplexy is the rule, and is commonly ushered in by convulsions which may involve the legs more markedly than the arms. The signs of the nervous lesion are bilateral. The pupils are strongly contracted at the onset, but before death may dilate widely. Vomiting is common. A rapid rise of temperature develops, and before death, which is the rule, a temperature of 108° F. may be reached.

Ventricular Hæmorrhage.—While usually secondary to intracerebral or subarachnoid hæmorrhage, primary effusion of blood into the ventricles has been recorded. Rapid onset and deep coma are the rule. There may be head retraction, intense rigidity of all four limbs, and periodical accesses of intense tonic and clonic spasm. Death ensues rapidly.

Subarachnoid (Meningeal) Hæmorrhage.—The usual source of hæmorrhage in this case is an aneurysm on the circle of Willis or upon one of the cerebral arteries in its neighbourhood (*vide* p. 594).

The hæmorrhage may take the form of slight and recurrent leakages, or of massive and rapidly fatal bleeding. This may occur at any age, and seems especially common in the third and fourth decades ; that is, at an earlier age than is the case with hæmorrhage in the substance of the hemisphere.

When leakage occurs there is intense occipital headache, stiffness of the neck, vomiting, vertigo, and occasionally epileptiform seizures. Consciousness may or may not be lost, according to the severity of the bleeding. A massive albuminuria may be present for a day or two from the onset, and is apt to lead to an erroneous diagnosis of renal disease, if its occasional occurrence with this lesion is not known. Signs of meningeal irritation ensue in non-fatal cases, and persist with mild fever for two or more weeks. Complete recovery is common in cases of this kind.

When bleeding is rapid and massive, the onset with headache is rapidly followed by deepening coma and death.

Other physical signs that may be observed are large subhyaloid hæmorrhages in the fundus of the eye, œdema of the optic discs, pupillary anomalies, and squint. Hemiplegia is absent, but there may be bilateral extensor plantar responses.

This type of hæmorrhage is more common than is usually supposed, and for this reason, and on account of the relatively early age of the subject, frequently escapes recognition.

In all cases of hæmorrhage into the subarachnoid space, lumbar puncture reveals abundant blood in the cerebrospinal fluid. When the blood-stained fluid is allowed to stand, the corpuscles settle, leaving a yellow supernatant serum. Lumbar puncture is, therefore, a diagnostic procedure of importance in cases of suspected subarachnoid hæmorrhage. During recovery high cell counts (lymphocytosis) may be obtained from the cerebrospinal fluid.

(*b*) **Embolism.**—The characteristic feature of embolic occlusion of an artery in the brain is the absolute suddenness of onset of symptoms. These vary in severity and type according to the size and the distribution of the vessel concerned. Emboli are most frequently arrested in the middle cerebral artery or one of its branches. When the main trunk is occluded, a large region of the affected hemisphere is rendered ischæmic, and the initial and residual symptoms resemble those due to hæmorrhage from this artery. Convulsions may occur at the moment of onset, consciousness is instantly lost, and signs of hemiplegia are present. With occlusion of a small cortical branch, headache, vertigo, and unilateral paræsthesiæ and weakness replace coma. Focal signs necessarily vary according to the region of brain affected. Thus aphasia, monoplegia, or a Jacksonian convulsion may be produced. Rapid recovery of function sometimes follows the temporary occlusion of such small vessels, but in the case of the main trunk of the middle cerebral artery, permanent and severe hemiplegia is to be expected. The anterior cerebral artery is very rarely involved, but the posterior cerebral artery not infrequently, with the production of hemianopia and sensory change. Rarely the internal carotid is blocked in this manner with the production of the so-called carotid hemiplegia, in which severe and permanent hemiplegia is associated with blindness of the eye on the side of the occlusion from blocking of the ophthalmic artery. In basilar embolism, signs of a brain-stem lesion with hyperpyrexia develop.

(*c*) **Thrombosis.**—Far more varied than the clinical pictures of hæmorrhage and embolism are those produced by occlusion, whether by spasm or by thrombus, of the cerebral arteries. While the two former necessarily produce acute disturbances of cerebral function of absolutely sudden onset, it is not surprising from what we know of the diffuse and progressive nature of degeneration of the arteries that it should give rise to both acute and chronic changes in the brain with corresponding acute and chronic symptoms. While the occlusion of a large cerebral artery, the middle cerebral for example, will be followed by an apoplectic seizure, differing only in detail from that occurring in cerebral hæmorrhage or embolism, the slow progress of degeneration in tiny cerebral arteries will be associated with a slowly progressive disturbance of cerebral functions, punctuated at intervals by more or less serious and transient " seizures " or " attacks " as some fresh and circumscribed region of the brain is temporarily or permanently deprived of its blood supply. These " seizures " may involve any of the known functions of the cerebral hemispheres according to the distribution of the artery involved. Thus more

or less transient hemianopia, sensory loss, hemiparesis, aphasia, or mental confusion may occur in numerous sequences and combinations, each separated by periods of remission of symptoms and more or less complete return to normal. If such restoration occurs before irreparable damage has ensued, then function resumes and paralytic manifestations clear up. In hypertensive encephalopathy (*vide* p. 593) transient focal signs, such as hemiplegia, may occur, and perhaps in this condition arterial spasm may play a part.

Generally, however, this kaleidoscopic symptomatology of diffuse cerebral arterial degeneration is accompanied by a slowly progressive deterioration of the highest cerebral functions and by an insidiously developing physical disability. Finally, a fatal hæmorrhage or softening may terminate the patient's existence, for it must be remembered that in atheroma we have a lesion which may result either in hæmorrhage or in occlusion, and it is not uncommon for the subject of one or more thrombotic seizures to be finally carried off by hæmorrhage. In the case of the middle cerebral artery, again the artery most frequently affected, the apoplexy and resulting hemiplegia do not differ essentially from those already described in association with hæmorrhage. Certain differences in the mode of onset are, however, characteristic of occlusion. There may be premonitory symptoms, both general and focal, and when occlusion is finally established, profound hemiplegia may develop over a period of one or more hours with little or no disturbance of consciousness. Not infrequently the subject retires to bed apparently in his usual health, to awake next morning fully conscious but with hemiplegia. In short, the disturbance of consciousness in thrombosis is apt to be less sudden in onset and less severe in degree than in a hæmorrhage causing a residual hemiplegia equally profound. Not uncommonly the onset is marked by a convulsion. In those cases where occlusion spreads proximally in a vessel from its distal end, gradually deepening coma and progressively increasing paralysis may occur. But in some instances a patient may pass from deep coma into a state of profound stupor with delirium, in which he may remain for several weeks until death ensues. On the whole, survival is more common in thrombosis than after hæmorrhage, and the fact of survival in a doubtful case is evidence in favour of thrombosis.

The residual focal symptoms which may follow occlusion and subsequent softening vary widely, according to the particular artery occluded. In the case of cortical branches, any of the known functions of the hemispheres may be affected. Occlusion of these branches of the anterior and posterior cerebral arteries is relatively uncommon except in the chronic cases above mentioned. In the case of the basilar artery the symptoms vary in detail according to the level of the occlusion and the extent of involvement of the lateral branches. The essential features, however, are cranial nerve palsies with crossed hemiplegic or crossed sensory disturbances, the so-called " alternating paralyses." The posterior inferior cerebellar artery is occasionally blocked and a characteristic syndrome results. Blocking of the cerebellar branches of the artery produces sudden acute ataxy on the side of the lesion, intense vertigo with forced movements, nystagmus, and vomiting; while the cutting off of the blood stream in the perforating branches which pass into the lateral region of the medulla produces : (i) a crossed hemianæsthesia for pain and temperature ; (ii) uncrossed symptoms referable to the fifth nerve (anæsthesia of the same side of the face), sixth nerve palsy (paresis of the external [lateral] rectus and diplopia), the glosso-pharyngeal-vagus-accessorius complex

(unilateral paresis of the palate, hoarseness of the voice), and paralysis of the sympathetic (enophthalmos, defective dilatation of the pupil in shade).

Slowly progressive disabilities related to arterial thrombosis have already been referred to, the essential lesions being multiple, recurrent, circumscribed areas of softening. Variable as the clinical expressions of this state of affairs may be, there are a few characteristic syndromes which may be briefly referred to.

Pseudo-bulbar Paralysis.—There is generally a history of two or more "strokes" which may have been comparatively mild, and without loss of consciousness or profound hemiplegia. The symptoms are caused by bilateral lesions in the region of the internal capsule, though in practically all cases of this kind cortical thromboses in the distribution of the middle cerebral artery are also present. They are those of bilateral hemiparesis with the addition of marked emotional overaction of the facial musculature, forced and uncontrollable weeping and laughter, and a gross disturbance of articulation. Considerable mental deterioration is also present in most instances.

Chronic Softening.—This may be taken to include the recurrence of softenings, involving any of the cortical areas and producing the variable series of transient visual, sensory, speech, motor, and mental disturbances already described, together with progressive mental deterioration.

Finally, a condition known as "arteriosclerotic muscular rigidity" has been described in which the patient develops a diffuse muscular rigidity, resembling that of paralysis agitans, with a characteristic gait in which he takes very short and shuffling steps. There may be no unequivocal signs of pyramidal tract involvement.

The Cerebrospinal Fluid.—Intracerebral hæmorrhage and thrombosis may produce no other change in the fluid than a rise of pressure, though in the subjects of cerebral arterial disease and chronic interstitial nephritis an excess of protein may occur quite apart from the cerebral lesion. When after hæmorrhage, blood reaches the ventricles, the cerebrospinal fluid may contain blood corpuscles, and when these are allowed to sediment the fluid may be yellow-tinged. A similar state of affairs may also follow extensive thrombosis, but on the whole such a finding suggests hæmorrhage as the condition present. In subarachnoid hæmorrhage, as is mentioned elsewhere, the fluid may be bright red from the onset, becoming clearer within a few days and yellowish in colour as the corpuscles disintegrate.

IV. Hemiplegia

The significance of the dual symptomatology of both recent and residual hemiplegia has already been discussed in the introductory chapter to this section, and further clinical details may now be added.

In coma, the signs of hemiplegia serve to differentiate apoplexy from the coma of various toxic states, endogenous or exogenous. The cheek on the affected side blows in and out loosely with each respiration. The limbs on that side also may be more flaccid than those of the opposite limb. Sometimes this is visible as the patient lies on his back, because the affected thigh loses its contours and flattens out. The head and eyes may show "conjugate deviation" towards the paralysed side—that is, away from the side of the lesion. This is an irritative phenomenon and transient in duration. Of even greater value than any of these signs is the presence on the hemiplegic side

of an extensor or Babinski plantar response, and of unilateral absence of the abdominal reflexes on the same side.

After consciousness is regained the phenomena of hemiplegia are fully revealed, and consist in a loss or impairment of unilateral voluntary movements. The face is paralysed in its lower half, the upper half being relatively little affected. The tongue is protruded towards the paralysed side, owing to the unantagonised action of the genio-hyoglossus (genioglossus) of the normal side.

The initial conjugate deviation of head and eyes towards the paralysed side gives place to a transient weakness, of some days' duration, of movement of both head and eyes towards the paralysed side. The movements of mastication and ordinary respiration are intact. At first, the arm and leg may be totally paralysed. The limbs are flaccid, but the tendon jerks by this time are brisker on the paralysed than on the normal side. The abdominal reflexes are lost on the paralysed side and the plantar response remains of the extensor type.

In partial hemiplegia the face is relatively slightly affected and the tongue may escape, while in the case of the limbs the arm is more severely affected than the leg.

Chronic Residual Hemiplegia.—After the passage of two or three weeks the hemiplegia undergoes certain changes, consisting in a degree of return of voluntary power and in the development of spasticity or hypertonus in the limb muscles. Recovery may be arrested at any stage, and a severe degree of residual paralysis persist. The condition in the limbs is one of loss, partial or complete, of movements, and not simple paralysis of individual muscles. The movements which return earliest and most completely in the arm are those of elevation and abduction of the shoulder, of flexion at the elbow, and of flexion of the fingers and wrist. Extension at the elbow frequently remains feeble and restricted, while extension of wrist and digits and, still more, isolated movements of the digits commonly remain absent. Thus an individual with a grasp of fair power may have no other useful movement of the hand or fingers whatever. In the leg, extension at hip and knee and plantar flexion of foot and toes return earliest and most completely, and may be of sufficient power to enable the patient to stand at a time when flexion at hip and knee are feeble and restricted, and there is no trace of dorsiflexion of foot or toes. Indeed, these last two movements frequently remain permanently absent.

The spasticity, like the return of voluntary movement, is selective in incidence, appearing in the adductors and flexors of the upper arm and in the extensors and plantar flexors of the lower, that is, in the muscles which become the strongest in the limbs. The spasticity, however, handicaps the activity of these predominant movements and renders them slow and clumsy.

It follows that the hemiplegic subject takes up a characteristic posture when standing, with the arm flexed and adducted, and the leg extended and the foot plantar flexed. In walking, owing to weakness of flexion and dorsiflexion, the affected leg is circumducted from the hip and the toe often drags.

Another feature in this phase is the appearance of the so-called associated reactions. Any forcible voluntary contraction of the muscles on the normal side, or such semi-voluntary movements as yawning or stretching, give rise to sudden accesses of tonic spasm in the paralysed arm and leg, and this spasm leads to the taking up of a fresh attitude of the limb while the move-

ment evoking it lasts. Thus in yawning, the arm usually rises up before the patient's face and the wrist and fingers extend. These activities are wholly involuntary and cannot be reproduced at will by the patient. The tendon reflexes in the affected limbs become extremely brisk, and the phenomena of knee and ankle clonus may appear. In some cases the abdominal reflexes on the hemiplegic side ultimately return, but the plantar response remains permanently of the extensor or Babinski type.

Finally, in long-standing cases some degree of secondary fibrous change takes place in the inactive muscles and the posture may become fixed, but the leg never goes into flexion contracture in an uncomplicated case of hemiplegia without spinal-cord lesions.

V. Diagnosis

The association of coma with acute cerebral vascular lesions renders diagnosis a matter of difficulty when the subject is found unconscious and nothing is known of the rapidity or mode of onset. Sudden onset—that is, apoplexy—is practically always indicative of a cerebral vascular lesion.

The various causes of coma may be briefly discussed under the headings of (*a*) toxæmic, (*b*) post-epileptic, (*c*) traumatic, and (*d*) cerebral lesions other than trauma.

(*a*) **Toxæmic.**—In all cases of this nature the coma is rarely as profound as after a cerebral hæmorrhage, and signs of *unilateral* cerebral lesions are wanting. In uræmia the subject may be of such an age and general condition as to make cerebral vascular disease probable. Hence the presence of albumin, blood, and casts in the urine does not necessarily exclude vascular disease as a responsible cause. In uræmia, however, coma is not so profound, some response to stimulation can usually be obtained, the tendon reflexes are obtainable, muscular flaccidity and incontinence of urine or fæces are not present, and the plantar responses are usually flexor. However, within a brief period of a uræmic convulsion the tendon reflexes may be lost and the plantar responses may be of Babinski type, but these signs are bilateral and very transient.

In *diabetes* the examination of the urine makes diagnosis easy. The reflexes are normal, unless a pre-existing diabetic neuritis has led to loss of knee and ankle jerks.

In *opium poisoning* the skin is cold and damp. Respiration and the pulse are slow and feeble. The reflexes are commonly stated to be normal, but in this, as in other forms of narcotic poisoning, the tendon reflexes may be lost and the plantar responses of Babinski type. These signs when present are bilateral. In opium poisoning the pin-point contraction of the pupils is of diagnostic significance. In cholæmia and delayed chloroform poisoning the plantar responses are commonly of the extensor type, and in rare cases signs of a unilateral cerebral disturbance may be present. Hence in the absence of a history of previous symptoms and of mode of onset diagnosis may be difficult.

(*b*) **Post-epileptic Coma.**—For the period of a few minutes after all generalised epileptiform convulsion, the pupils are inactive to light, the corneal reflexes absent, the tendon reflexes abolished, and the plantar responses of Babinski type. These phenomena are transient, there are no signs of unilateral cerebral lesion, and certain features indicative of convulsion may be present,

e.g., tongue biting, incontinence, the presence of old scars of injuries sustained in previous fits.

(*c*) **Traumatic Cerebral Lesions.**— In cerebral concussion the patient loses consciousness instantly at the moment of injury. The condition is one of collapse: low blood pressure, weak pulse, slow and shallow respiration, pale face, dilated pupils, and flaccid muscles. As coma passes off, signs of irritability and restlessness appear: the pulse is forceful, respiration becomes deeper, and the temperature may rise two or more degrees. Finally, consciousness is regained with the appearance of headache.

In extra-dural meningeal hæmorrhage the concussed patient regains consciousness, and then, with the rise of blood pressure, hæmorrhage begins, and the symptoms of compression of the brain develop within the course of a few hours. The patient passes through a phase of cerebral irritation back into coma. As pressure rises within the skull, unilateral symptoms, first irritative and then paralytic, make their appearance: Jacksonian fits, followed by hemiparesis with corresponding reflex changes. Other focal signs appear according to the region in which compression is most severe.

The development and clinical picture of chronic subdural hæmatoma has been dealt with in the chapter on the meninges.

(*d*) **Non-traumatic Cerebral Lesions.**—The age and general condition of the subject may afford valuable information as to the nature of the lesion. Thus endocarditis and mitral stenosis are associated with embolism and occur in young subjects, particularly in women.

A mode of onset suggestive of cerebral thrombosis in a young adult, particularly a male, indicates syphilitic endarteritis.

In elderly persons with high blood pressure, cardiac hypertrophy and signs of interstitial nephritis, either hæmorrhage or thrombosis may be in question. A differentiation may be impossible, but the mode of onset often enables a correct diagnosis to be made.

As to mode of onset, embolism is characterised by absolute suddenness without prodromal symptoms. In hæmorrhage, transient premonitory symptoms of the type already described may be present. Coma is deep, and the general appearance of the patient has been discussed above. In thrombosis, onset is less sudden. The hemiplegia may begin to appear before consciousness is lost, and epileptiform convulsions may usher in the development of the lesion. Coma may be absent, or may be transient and not deep. Recovery of consciousness and survival is presumptive evidence in favour of thrombosis as opposed to hæmorrhage. Again, an onset during sleep after a day of fatigue is more common in thrombosis than in hæmorrhage, which is sometimes associated with physical effort. A sudden onset of coma with death within a few moments is practically never due to a cerebral lesion, but to coronary thrombosis and cessation of the heart beat.

The appearance of intense headache, followed rapidly by coma and death, is commonly due to subarachnoid hæmorrhage from rupture of a basal aneurysm, and may occur in otherwise healthy subjects of any age.

Apart from primary cerebral vascular disease, hæmorrhage into the brain may occur in a variety of conditions. Thus hæmorrhage into a growing glioma may be rapidly fatal, or it may be a terminal incident in acute leukæmia and other altered blood states. In certain acute infections such as diphtheria, and in septic conditions such as puerperal sepsis, embolism and thrombosis may occur.

VI. Prognosis

In intracerebral hæmorrhage, death occurs in a large proportion of cases within forty-eight hours. Survival is more likely after thrombosis, but here ultimate prognosis as to life is influenced by the persistence of the factors which gave rise to the original cerebral lesion. In arterial disease the subject remains a precarious life, always liable to recurrent "strokes." In some cases of atheroma with softening, when the patient's mode of life is carefully regulated, a useful if restricted existence may be enjoyed for several years without recurrence of cerebral lesions. In syphilitic thrombosis, on the other hand, prognosis is determined by the thoroughness with which antisyphilitic measures are initiated and carried out. In the matter of recovery from hemiplegia, prognosis is gravest after hæmorrhage, since actual destruction of tissue has occurred. In transient occlusion, from thrombosis or embolism, complete or almost complete recovery of function sometimes occurs, but it is usually found that the fine purposive movements of an affected hand are not completely regained in any but the most fugitive hemiplegias.

In subarachnoid hæmorrhage, free and continued hæmorrhage may prove rapidly fatal. In many cases the bleeding is less copious and of brief duration. In these circumstances recovery is common. The liability to recurrent bleeding is greatest in the fortnight following the original subarachnoid hæmorrhage. In many patients recovery is followed by complete restoration to normal health and later recurrence does not occur, but it is impossible to estimate the expectation of life in the individual case.

VII. Treatment

The recognition of arterial disease in an elderly person at a time when no manifestation of involvement of the cerebral vessels is present calls for some circumspection in the matter of treatment. Many persons in whom routine examination has revealed the presence of a high blood pressure are made utterly miserable in their remaining years by severe restrictive measures of uncertain value, accompanied by unwise and dismal forebodings on the part of their medical advisers. If the patient cannot be induced to lead a regular life and to exercise moderation in all activities without being put in perpetual dread of apoplexy, his medical adviser will probably prefer to leave him some measure of peace of mind, even at the risk that something less than an ideal regime of life may be continued. Once, however, definite indications of cerebral vascular disease have appeared, such as headache, vertigo, paræsthesiæ, or other transient focal disturbances of function, or after a definite structural lesion, the patient must face a restricted life. Fatigue, excess of food or alcohol are all strongly contraindicated.

Whether systematic attempts to lower the level of blood pressure are effective, or if effective of value, is doubtful. But factors likely to cause wide fluctuations of blood pressure, the common immediate cause of both hæmorrhage and thrombosis, are to be avoided.

In both hæmorrhage and thrombosis the patient must be kept at rest. In unequivocal cases of hæmorrhage when there is a strongly acting heart, a flushed face and an incompressible pulse, early venesection may be of value, from 10 to 15 oz. of blood being removed. But a soft, irregular pulse and the presence of any doubt as to whether the case is one of hæmorrhage or thrombosis strongly contraindicate venesection.

Again, in cases of hæmorrhage early and free purgation has been thought to be of value because of the dilatation of the abdominal vessels which it produces, and croton oil is used for the purpose.

In thrombosis the use of cardiac stimulants is indicated, and the administration of easily assimilable foods may be attempted.

The treatment of subarachnoid hæmorrhage depends largely upon the severity of the case. When consciousness is not lost, or only briefly, we may assume that no considerable increase of intracranial pressure is present, and therefore the diagnostic lumbar puncture having been made, there is no indication to repeat the procedure. In these circumstances, the prime necessity is to keep the patient as quiet as possible and to relieve the headache and pain in the neck and back associated with meningeal irritation. For this purpose morphia may be necessary for several days, though milder sedatives may serve in some cases. When there is deep or prolonged coma, repeated drainage of the subarachnoid space by lumbar puncture may be indicated. The depth of coma and the pulse-rate must be studied to determine the frequency which is best in any given case. During recovery, restlessness and mental confusion may persist for three or more weeks and may require the use of luminal or other comparable sedatives. In some cases subsequent ligature of the carotid is indicated.

In all cases the possibility of retention of urine should be borne in mind, and what appears to be simple incontinence of urine is commonly overflow from a distended bladder.

Pulmonary congestion and broncho-pneumonia carry off many patients who survive the immediate shock of the cerebral lesion. This complication may be figuratively spoken of as "a bedsore in the lung," and like the bedsores which may develop elsewhere, is to be prevented by careful changes in the position of the patient in bed.

Once the period of coma is passed and the presence of severe hemiplegia is revealed, the careful prevention of contractures and deformities must be taken in hand without delay. The leg must be kept extended, adducted, and rotated in, and the foot supported. The hand and digits must not be allowed to lie in a constant posture of flexion, which will invariably be the case unless active measures are taken to prevent it. Careful and gentle passive movements of the limbs may be begun as soon as convalescence from the cerebral lesion is established, but it is probable that premature active use of partially paralysed limbs may promote the development of spasticity. After the fourth or fifth week, however, if power is returning into the limbs, some active exercise is essential. Electrical stimulation at any stage, early or late, is strongly contraindicated. In transient hemiplegia where complete recovery is in sight it is not necessary, while in permanent residual cases it aggravates spasticity.

For the hand in old spastic hemiplegia, active use of the fingers is the best form of local treatment, and exercises to meet the conditions present are readily devised. In such cases the degree of ultimate recovery depends more upon the assiduity with which the patient carries out such exercises than upon any other factor, and massage is not an adequate substitute for them. When the fingers have regained some movement, the handling of dominoes and other small objects is a useful form of re-education. It is clear, however, that all measures of the kind are of value only in subjects in otherwise good general health and with normal mental faculties.

DISTURBANCES OF SPEECH

Articulate speech and writing (and, to a less degree, gesture) are highly specialised forms of movement by which the individual expresses his thoughts. Spoken and written words are the symbols employed for this purpose, and like other movements, those of speech and writing are ultimately under the directive influence of sensory impressions. Some simple general ideas of the speech function and its disorders in disease may be gained by pursuing the analogy with movement still further.

Co-ordinated movement may be disordered by a cutting off of the sensory impressions which normally reach the cerebral sensory cortex, or by a failure to integrate these sensations when they arrive. In these circumstances the disorder of movement resulting is not in the nature of weakness or loss of movement, but is an inco-ordination ; movements can still be made, but they are wrong movements. If the subject's eyes be closed he is not aware of the disorder and can make no attempt to correct it.

When the efferent or executive side of the mechanism of co-ordinated movement is damaged, movements are weakened or lost. This loss will depend for its character upon the particular level of the motor mechanism which is out of order. The lesion may involve either the lower or the upper motor neurone with results appropriate to the seat of the lesion in each case. However, the lesion may involve even higher levels of the mechanism, the so-called eupraxic centres. When this happens there is no paralysis in the ordinary sense of the term, but the subject is unable to initiate certain purposive movements at will.

Further, in the case of any given function it is always its most complex expression which is earliest and most severely damaged, as was mentioned in the introductory chapter to this section.

In speech we are dealing with a higher grade of cerebral activity than the mere performance of co-ordinated movements, because the auditory and visual impressions received when the subject hears spoken or sees written words have acquired a symbolic meaning ; they have become the coinage of thought. Similarly, the movements of spoken and written speech, and to a less extent those of gesture, have also acquired a symbolic value under the influence of these highly elaborated visual and auditory impressions. This investing of sensory impressions and of movements with symbolic significance is the result of intellectual processes, and therefore there are anatomical, physiological, and psychological aspects of the speech function : anatomical in that the neurones concerned in the receptive and expressive functions described above are grouped in certain more or less well-defined cortical areas, physiological in respect of the specific activities of these neurones, and psychological in respect of the mental processes which are manifested in speech. Thought is possible without words, but for the expression and exchange of thought they are clearly essential.

The groups of neurones concerned in the endowment of visual and auditory impressions with symbolic value, and those which initiate the movements of written and spoken speech, are all localised in the left cerebral hemisphere, in what for purposes of exposition are spoken of as centres. The so-called auditory word centre is situated in the first temporal convolution, the visual word centre in the angular and supramarginal (inferior parietal) convolutions,

and the motor speech centres at the posterior ends of the second frontal convolution (writing) and third frontal convolution (speech). The latter is often known as Broca's area.

These cortical areas are intimately connected by association fibres in the subcortex, and together are included in a roughly quadrilateral region on the convexity of the hemisphere. As is to be expected, lesions involving the anterior portion of this region tend to impair executive speech functions predominantly, those involving the posterior part the receptive aspects of speech (see Fig. 25, p. 576).

In left-handed persons the speech centres may lie in the right hemisphere and lesions in this hemisphere may be followed by disorders of speech of the kind under consideration, while lesions of the left hemisphere produce no such disorders. Occasionally, also, a right-handed member of a stock in which left-handedness is known to be common may show speech disorders after a lesion of the right hemisphere. Such an individual is said to have come from a "right-brained stock." The converse condition is also known to occur.

Morbid Anatomy and Pathogenesis.—Lesions of any nature involving these cortical regions will produce disturbances of speech function of a degree and kind proportionate to their severity and topography. The commonest cause of such lesions is atheroma of the cortical branches of the left middle cerebral artery, with resulting arterial occlusion and thrombosis. Speech defects are therefore a frequent symptom in vascular lesions within the territory of this artery. Tumour and abscess within the same region will produce comparable defects.

Symptomatology.—**Expressive or Motor Aphasia.**—In this we have a greater or less degree of loss of the power of expressing thought in speech. The speech musculature is not paralysed and can still carry out all movements other than those of articulate speech, but the latter are lost or greatly reduced in number. The loss may vary from a loss of names (nominal aphasia) to a loss of all but a few recurrent utterances, such as "Yes," "No," or "Thank you." Such words as are uttered are perfectly articulated, except in very fresh lesions, when some dysarthria may be present. In nominal aphasia the patient can recognise an object held before him but cannot name it. Instead, he describes it, speaking of a pencil as "what you write with." In conversation he has to adopt similar periphrases. Simple questions on long-familiar topics may be answered correctly, but more complex ones involving the use of words in thinking (internal speech) may find the patient unable to express himself. It is sometimes noticed that a patient who is reduced to a few recurring utterances can, under the influence of emotion, speak volubly or even sing the words of a song, the expression of emotion being less severely impaired than that of thought.

Lesions having this effect commonly involve Broca's convolution, which lies at the posterior end of the third left frontal convolution and at the foot of the ascending frontal (precentral) convolution.

When the posterior end of the second frontal convolution is involved, the movements of writing are impaired or lost, a condition known as "agraphia." Here, as in the case of the articulatory muscles, all other movements of the hand and fingers may be intact.

These two disturbances of expressive speech may be present simultaneously, or either may be found alone.

Clinically it is commonly, though not invariably, found that persons with

motor aphasia cannot understand what they read; they are "word blind," and this even in the absence of any lesion of the visual word centre. This symptom is supposed to be due to an inability of many persons to read with understanding unless they can "say over" silently what they read. The motor aphasic cannot do this, and hence is unable to pick up the meaning of the words he sees.

Sensory or Receptive Aphasia.—Here we have a defect of comprehension of spoken or of written speech (word deafness, or word blindness) in the absence of deafness or blindness. The executive mechanism of speech in uncomplicated cases remains intact. Since auditory and visual impressions have lost their appropriate symbolic value for the patient, not only does he not understand what he hears or reads, but the activation of the executive mechanism is disordered, and he uses wrong words, mixes up the words in a sentence, and may talk an unintelligible jargon. To return to the analogy of movement, we may say that the patient can make speech movements but they are wrong movements.

Almost pure word deafness or word blindness may exist alone, but the two are more commonly present together. Similarly, in the majority of instances lesions are so placed as to involve both the receptive and the expressive parts of the speech mechanism, so that so-called mixed forms of aphasia are found. Lesions involving any of the so-called speech centres tend to interrupt association paths between the different parts of the cortical representation of speech, and so produce these complex disturbances.

The patient's comprehension of spoken and written speech may be tested by giving him oral and written orders of a simple character and noting his response. His powers of expression are tested by asking spoken or written questions which demand verbal or written responses, by asking him to name and identify objects shown to him or to use them appropriately.

Apraxia and Agnosia.—In certain cortical lesions immediately anterior to the cerebral motor cortex, not only may motor aphasia or agraphia result, but there may also be an inability to perform other purposive movements to order, and this although the muscles concerned are not paralysed for other movements, or for the same movements when carried out spontaneously. For defects of this type, in which motor aphasia is included, the term "apraxia" has been coined. The subject of motor apraxia cannot carry out certain complex movements to order and cannot handle familiar objects, such as a pipe, a cigarette, or a key, appropriately, although he is aware of their nature and proper use.

On the afferent side also not only may the significance of words heard be lost but objects perfectly seen may not be identified by the subject, or are wrongly identified. This defect is spoken of as "agnosia," and word deafness and word blindness are special varieties of agnosia.

All these elaborations of received sensory impressions and the corresponding performance of purposive movements are functions of cortical cells, and hence the various expressions of apraxia and agnosia are seen in the subjects of cortical lesions.

Dysarthria.—In addition to the disorders of speech already considered, it is clear that paralysis or inco-ordination of the speech musculature will render articulation difficult or impossible.

Such defects may be classified under the same headings as other disorders of movement. Thus in spastic conditions of the musculature; *e.g.*, in

pseudobulbar paralysis and in spastic forms of chronic bulbar palsy the patient may be reduced to making wholly inarticulate sounds (anarthria); in general paralysis articulation is slurred; in cerebellar disturbances such as follow lesions of the cerebellum and as seen in disseminated sclerosis and Friedreich's ataxy, the articulation is of the scanning type. Finally, in lower motor neurone paralysis and in muscular diseases (myasthenia gravis, myopathy) defects of voice production as well as of articulation may occur. The features of these various forms of articulatory defect are considered under the heading of the diseases in which they occur and need not be further described. Their treatment is that of the causative condition.

Stammering.—This impediment of speech is of quite another order from the defects of speech so far considered. It is frequently inherited and associated with a neuropathic diathesis. It appears in early childhood, and is by nature allied to the tics and the psychoneuroses. It is, therefore, not due to any local disease of the neuromuscular mechanism of speech but to a disorder of voluntary co-ordination between the respiratory, the laryngeal, and the labio-lingual components of this mechanism. The general principles of treatment enunciated for the tics and psychoneuroses apply to the treatment of stammering, with the addition under trained supervision of breathing, singing, and reading exercises.

THE CEREBRAL PALSIES OF CHILDHOOD

Cerebral Diplegia

Under this heading are grouped a number of clinical conditions characterised by signs of bilateral affection of the cerebral hemispheres dating from birth.

Ætiology.—It is thought by some that agenesis or defective development of different systems of neurones, the latter occurring at varying periods of development, may be responsible for all the conditions included under this heading. It is probable, however, that disease processes during intrauterine life also play a part in their production.

The widely held view that cerebral injuries sustained during parturition play a part in the production of cerebral diplegia rests upon no sound clinical or pathological grounds. The child is frequently the first-born of its mother, and when abnormalities of labour and delivery are present these are as frequently of the nature of precipitate birth as of prolonged or difficult labour. Further, there is no pathological evidence that birth injuries stand in any relation to cerebral diplegia. On the contrary, there is every reason to conclude that antenatal factors are alone operative.

Morbid Anatomy.—Amongst the various pathological conditions found in the brains of subjects of cerebral palsies of congenital origin is *atrophic sclerosis*. The convolutions are shrunken, with wide intervening sulci. The whole or part only of the cerebral hemisphere may be affected. Microscopically, there is found a marked glial proliferation and defective myelinisation of the nerve fibres.

Symptomatology.—The following clinical types have been described :—

1. *The Spastic Group.*—There is generalised muscular rigidity, usually predominating in and sometimes confined to the lower limbs. These are rigidly extended and adducted, and may be crossed. When rigidity allows of

their elicitation, the knee and ankle jerks are found to be increased and the plantar responses of the extensor type. The abdominal reflexes are generally retained. This condition is found in degrees of severity varying from slight rigidity and disorder of gait to intense adductor spasm and rigidity with "scissors gait" and an inability to place the heels on the ground. The arms may be intact and the patient's mental development normal. This is the clinical picture of what is known as Little's disease. In other cases the arms also are involved and there is a varying degree of mental deficiency and, sometimes, epilepsy.

2. *Bilateral Athetosis.*—The limb and facial musculature is the seat of more or less continuous writhing movements ("mobile spasm") which are aggravated and spread during all attempts at voluntary movement. The muscles of articulation and mastication may be involved. These phenomena are minimal at birth and tend to increase in severity later in childhood. There is a varying degree of associated mental defect.

3. *Choreiform Group.*—This is characterised by the presence of jerky, rapid involuntary movements of choreiform type, involving the limb and articulatory musculature. There may be no signs of pyramidal involvement, and in some instances no mental defect.

Treatment.—The only cases for which anything can be achieved by treatment are those in which the legs are spastic, but the arms normal and the child's mental development good. In these, it is sometimes possible by judicious tenotomy and carefully planned motor nerve division to overcome muscular spasm and contracture. When this has been done, the child may be educated to walk in a more normal fashion than was before possible. A period of institutional treatment in a special school for such children, where physical measures accompanied by judicious encouragement and training are available, will yield good results even in gravely disabled cases when intelligence is good.

Further, some cases of this kind do undergo a measure of spontaneous improvement as they approach adolescence.

Infantile Hemiplegia

Rarely this is congenital in origin and due to the causes we have considered in connection with cerebral diplegia. When cerebral injuries (compression or hæmorrhage) are sustained at birth, the resulting disability is a hemiplegia, and some cases of infantile hemiplegia arise in this way. The common variety, however, makes its appearance suddenly during the early years of infancy in association with one or other of the acute specific infections. In these circumstances its origin may be embolic, or due to hæmorrhage or thrombosis, to a cortical thrombo-phlebitis, or, finally, to a localised focus of encephalitis. The infections in question are measles, mumps, scarlet fever, whooping-cough, typhoid fever, and poliomyelitis.

Symptomatology.—There is a sudden onset with generalised convulsions and coma which may persist for as long as twenty-four hours. In some instances the convulsions are unilateral. A general febrile reaction accompanies these symptoms. On recovery the child is found to have a hemiplegia of varying severity. Sometimes aphasia results. Subsequently there may be partial or complete recovery, or a varying degree of residual hemiplegia and speech defect. Involuntary movements of athetotic variety are liable to appear in

the affected musculature. Other common sequels are mental deficiency and epilepsy.

Treatment.—This consists in the treatment of the residual hemiplegia, which is conducted on the lines described in the case of adult hemiplegia.

CEREBRAL THROMBO-PHLEBITIS: SINUS THROMBOSIS

Thrombosis of the cerebral venous sinuses may occur in marasmic infants, as a terminal phenomenon, in association with middle ear suppuration and with infections of the face. Attention has recently been drawn to the occurrence of hydrocephalus as a result of superior longitudinal sinus thrombosis in children with middle ear disease, and the occurrence of hemiplegia and other cerebral symptoms in women during the lying-in period or after abortion has also been correlated with thrombosis of this sinus, with or without accompanying thrombosis of cortical veins. Gowers suggested that some cases of infantile hemiplegia with an onset with convulsions and coma might be due to thrombosis of the superior longitudinal sinus and cortical veins. Cerebral sinus thrombosis in women during the puerperium probably arises in the following way. The pelvic veins have long been known to anatomists to communicate with the vertebral system of veins and this with the cerebral dural sinuses. If, as commonly happens in the circumstances named, the patient is wearing a tight binder and has thrombosis in the pelvic veins, any fragment of clot detached from the latter may find its way, not as commonly into the caval system of veins, but into the vertebral veins whence it may reach the superior longitudinal sinus. Here it may become attached to the sinus wall, or to the wall of one of the tributary cortical veins, where it forms the nucleus of a larger clot and may set up a local inflammation of the vessel wall (cerebral thrombo-phlebitis). Thus during the second week of the puerperium the signs and symptoms of this cerebral complication may develop.

Again, in middle ear disease in children, superior longitudinal sinus thrombosis may ensue, and may obstruct the re-absorption of cerebrospinal fluid, via the Pacchionian bodies, into the venous system. A hydrocephalus may thus be produced. The carriage of infection by venous channels from the face may lead to cavernous sinus thrombosis.

Symptomatology.—The symptoms peculiar to thrombosis of the different sinuses were fully described by Gowers as long as fifty years ago, and may be summarised as follows :—

Superior Longitudinal Sinuses.—A condition of stupor leading to coma may develop, and there are headache, sickness, and papillœdema. When the cortical veins become subsequently involved there ensue convulsions and hemiplegia. If, as may happen in the case of lying-in women and by the mechanism already described, the veins are involved earlier than the sinus, the onset is with convulsions, coma, and hemiplegia. Death may result, or recovery with residual hemiparesis or without any residual disability. Thrombosis of veins in the pelvis precede the cerebral complication. In children with middle ear disease, the development of superior longitudinal sinus thrombosis is indicated by headache and papillœdema, and sometimes by stupor or coma.

Cavernous Sinus.—This is commonly infective and the patient is clearly

gravely ill and with a high temperature. There is proptosis, œdema of the eyelids, cranial nerve palsies (3, 4, 6), and some œdema of the optic disc.

Diagnosis.—It is hydrocephalus (otitic hydrocephalus) associated with middle ear disease and the sinus and cortical venous thrombosis of lying-in women that constitute the main neurological problems of sinus thrombosis. In the former, the development of headache and other symptoms of raised intracranial tension raises the question of abscess, meningitis, or hydrocephalus. In the last named, the cerebrospinal fluid is under increased pressure but remains normal in composition. In meningitis and abscess there is usually some meningeal reaction (lymphocytosis, etc.) in this fluid. The development of coma, hemiplegia, or convulsions during the puerperium should lead the observer to suspect sinus thrombosis and to look for evidence of pelvic or femoral vein thrombosis.

Treatment.—When there is reason to suspect thrombosis of pelvic veins after parturition or abortion the patient should be propped up in bed and the abdominal binder loosened. For raised intracranial tension the steps described on page 593 should be adopted, and for convulsions those described in connection with status epilepticus. For otitic hydrocephalus repeated lumbar puncture may suffice, it being assumed that the original focus of infection in the ear has been dealt with.

PARALYSIS AGITANS (PARKINSON'S DISEASE)

Definition.—A slowly developing malady of elderly persons characterised by diffuse muscular rigidity, tremor, slowness and limitation of the range of movement, and by a peculiar stance and gait. In his original account (London, 1817), Parkinson described it as consisting of "involuntary tremulous motion, with lessened muscular power, in parts not in action and even when supported; with a propensity to bend the trunk forwards, and to pass from a walking to a running pace, the senses and intellects being uninjured."

Ætiology.—Nothing certain is known of the causation of this malady. It is rare before the fifth decade of life, and from this period onwards the case incidence steadily increases. Males are more frequently affected than females. This age and sex incidence are also those of cerebral arterial degeneration. In this connection it is noteworthy that a raised blood pressure is unusual in paralysis agitans, while gross cerebral lesions of vascular origin (hæmorrhage or thrombosis) very rarely occur in the subjects of this disease. As is the case with all other chronic maladies of the nervous system of obscure ætiology, cold, stress of all forms, trauma, and infection have been invoked as causative or predisposing factors. There is, however, no conclusive evidence that any of them stand in any other than a relationship of coincidence with the apparent onset of the malady. The view that trauma may determine the onset and site of initial symptoms has been handed on from writer to writer, but its reiteration is its most substantial claim to acceptance.

Morbid Anatomy.—The essential lesions are found in the neighbourhood of the corpus striatum and subthalamic region, and they consist in degeneration and necrosis of nerve cells and fibres. There may be actual lacunæ round the vessels. The process is essentially a senile one, though localised.

Symptomatology.—The onset is insidious and muscular rigidity is commonly the earliest manifestation. The normal play of expression vanishes from

the face, which assumes a fixed, mask-like appearance. The natural swing of the trunk and arms in walking diminishes, the gait assumes a gliding monotonous character, and the arm on the earlier affected side ceases to swing and lies adducted and slightly flexed at the side of the trunk. The patient tends to assume an attitude of slight flexion, the head and back bent forwards, and the legs not fully extended either in standing or walking. At first the affection of the limbs is unilateral, but usually within two years the limb musculature of both sides is involved. All movements become slow and restricted in range. The patient experiences difficulty in rising from a chair, in shaving, and in dressing. Usually within a few months of onset the arm first affected becomes the seat of a fine rhythmic tremor, which may be present when the limb is at rest and fully supported, or appear only when it is in action. Even then, in rapid movements, especially to-and-fro movements, it tends momentarily to cease. It is increased by fatigue or emotion. The leg is next affected and the head or the lower jaw may be tremulous. Sometimes tremor appears first in the index finger, which then makes a "pill rolling" movement on the thumb. The pupillary and extrinsic ocular movements are intact. The tendon jerks may either be increased or they may remain normal. The abdominal reflexes persist intact, and the plantar responses also remain normal. There is no objective sensory loss, but the patient may complain of fugitive paræsthesiæ and of pains in back and shoulders. Gradually with the increase of muscular rigidity the activities of the patient are progressively restricted. The gait assumes a rapid short-stepped character, the so-called festinant gait. The patient often breaks into a shuffling trot, and unless he can pull himself up is apt to topple forwards. Occasionally, also, there is a tendency to step backwards in the same way. These phenomena are known as propulsion and retropulsion. The patient has difficulty in changing his position when sitting or lying in bed, and may have to be moved at frequent intervals to relieve the numerous pains and discomforts which ensue from immobility. There is a clinical type in which tremor is the initial symptom and predominates throughout the course of the malady. Rigidity is present in relatively slight degree and the Parkinsonian facies may be late in appearing. In such cases the tremor is more ample and disabling than in the rigid cases.

Ultimately, the patient becomes bedridden and helpless. He tends to have periods of stupor, muscular rigidity renders mastication and articulation difficult, and speech may become unintelligible. Sometimes, despite Parkinson's dictum, a progressive mental deterioration sets in, and the last months of life are passed in stupor and anarthria.

When life is not cut short by some intercurrent affection, the disease may take ten or more years to run its full course; but comparatively few patients survive so long, the majority dying of broncho-pneumonia before the final stage, with its mental hebetude, sets in.

The characteristic lack of expressional and of associated movements in the disease is largely, if not entirely, due to the muscular rigidity which damps down and finally extinguishes all but the most essential and purely voluntary elements in movement. In a few cases rigidity reaches an extreme degree, and tremor may be entirely absent, the so-called paralysis agitans sine agitatione. In other cases, again, tremor predominates and is free and ample in range, while rigidity, although always present in tremulous muscles, is minimal.

Diagnosis.—The onset is so gradual that the disease has usually been

present for a year or more before recognition. In its initial stages it is most readily identified by the careful inspection of the patient as he approaches the examiner. In these circumstances the fixed, mask-like facies, the short-stepped gliding gait, the immobility of the affected arm as the patient moves, and the slow dawning and passing of such expressive movements as the face may show, all go to make up a striking clinical picture, which is compounded of such slight deviations from the normal that a systematic examination of the patient may fail to reveal what has not been recognised at first sight.

The absence of qualitative alterations in the reflexes or of objective sensory loss are negative signs confirmatory of the presence of the disease.

A so-called Parkinsonian state closely resembling paralysis agitans frequently follows recovery from an attack of encephalitis lethargica. The points of differential diagnosis are that in post-encephalitic paralysis agitans the patient may be of any age from early childhood onwards; tremor of the limbs is not so early nor so prominent a symptom, but there is usually tremor of the closed eyelids and of the protruded tongue; there may be anomalies of pupillary reaction and of ocular movement (loss of convergence and of accommodation); the skin of the face is greasy, and profuse salivation and dribbling are common. Frequently bizarre and complicated involuntary movements of face, tongue, trunk, or limb muscles are present, or striking disorders of respiratory rhythm and force. In many cases a history of an acute attack of encephalitis may be obtained.

Treatment.—The ultimate end of this fatal malady cannot be averted, but—at least in its earlier stages—some relief can often be given both to the rigidity and—though to a less degree—to the tremor. The drugs of choice are belladonna, stramonium, and hyoscine hydrobromide. One or other of these is given in increasing doses until an optimal result is obtained, and the drug then continued at this—or a slightly lower—level of dosage. Hyoscine probably gives more relief from tremor than the other drugs. It may be given by mouth in doses of from $\frac{1}{200}$ to $\frac{1}{100}$ gr. three times daily, and many patients get considerable subjective relief when this is combined with benzedrine sulphate. The tolerance of the latter drug and its effects seem to vary widely from patient to patient, and it is best to begin with 10 mg. twice a day (morning and early afternoon), or this dosage can be subdivided into four doses of 5 mg. over the first half of the day period. Some subjects do well on larger doses. Stramonium and belladonna may be given as tinctures (10 minims rising to 30 minims, t.d.s.) or in pill form. Many patients respond more markedly when, in addition to these drugs, they are given a morning dose (before breakfast) of benzedrine sulphate (5 to 10 mg.), half the latter dose being repeated before the midday meal.

Pains and sleeplessness can be treated as they arise. The subjects of paralysis agitans do not tolerate the barbiturates well except in small doses.

In the final stage of extreme rigidity and immobility the patient is bed-ridden, and usually becomes extremely thin, and requires to have everything done for him.

HUNTINGTON'S CHOREA

Huntington's chorea is a rare malady of middle-aged and elderly persons, of slow onset, characterised by the development of choreiform movements of

head and neck, face, tongue, and limbs, and also by a progressive dementia. It is a heredo-familial disease, may be traced through several generations, and may occur in several members of a single generation. The movements resemble those of rheumatic chorea, but are usually not quite so sudden and jerky. The facial involvement may be severe and articulation may become unintelligible. The dementia is progressive. Maniacal outbursts and suicidal tendencies are common.

The disease runs a steadily progressive course and recovery is unknown. When no heredo-familial factors are present, we may speak of the condition as chronic progressive, or senile, chorea.

Under the name of " apoplectic chorea " we may mention a sequel of hæmorrhage into the region of the substantia nigra and corpus subthalamicum (subthalamic nucleus). The apoplectic seizure is followed by the development of intractable and severe choreiform movements of strictly unilateral distribution. Death from exhaustion after some weeks is the usual termination.

HEPATO-LENTICULAR DEGENERATION

Progressive Lenticular Degeneration.—This rare and fatal malady is characterised by the progressive development in adolescents or young adults of widespread tremor and rigidity of the musculature, defects of articulation and deglutition, spasmodic weeping and laughing, a slight degree of dementia, and by the absence in uncomplicated cases of any true paralysis or of those changes in the reflexes associated with pyramidal system lesions. Pathologically, the nervous lesion consists in a bilaterally symmetrical degeneration of the lenticular (lentiform) nuclei, and sometimes of other regions of the brain, and there is in addition portal cirrhosis of the liver. There may also be a deposit of pigment granules at the periphery of the cornea. It may occur in more than one member of a family. Its course is uninfluenced by treatment. It seems probable that the hepatic lesion precedes that of the brain.

CEREBRO-MACULAR DISEASE

(*Amaurotic Idiocy, Tay-Sachs Disease*)

A rare familial form of progressive cerebral degeneration, occurring chiefly in Russian Jews, and characterised by progressive paralysis and mental deterioration and by a peculiar form of macular change. Its causation is unknown.

Symptomatology.—The child is normal at birth and for some months subsequently. It then begins to become progressively weaker and apathetic and to show signs of visual impairment. Later, generalised muscular rigidity and blindness ensue, followed finally by coma, with or without convulsions, and death. Ophthalmoscopic examination reveals primary optic atrophy with a " cherry-red spot " surrounded by a pale halo at the macula.

Morbid Anatomy.—Microscopic examination of the brain reveals extensive degeneration changes in the nerve cells and their processes, with a glial reaction. The retinal ganglion cells are similarly affected.

Other comparable familial forms (juvenile and adolescent) of progressive

cerebral degeneration, with and without macular changes, and not confined to the Jewish race, have also been described. There is no treatment for any of these conditions.

TOXIC ENCEPHALITIS

Acute inflammation of the brain occurs under varying conditions, and it may be suppurative or non-suppurative. The suppurative variety has been dealt with (*vide* p. 587) under the heading of Cerebral Abscess. Of the non-suppurative variety almost all cases are examples of virus infection of the nervous system, and these are dealt with under that heading on page 623. There remain for consideration here rare cases of toxic origin.

Wernicke's Polioencephalitis Hæmorrhagica Superior.—In this the symptoms are referable to a lesion of the peri-aqueductal grey matter ; viz., ocular palsies, drowsiness, and alternating paralyses. It is probable that this condition is a degenerative rather than an inflammatory process. There is a marked proliferation of small blood vessels, from which minute hæmorrhages occur, and also nerve-cell degeneration and glial proliferation.

After the administration of the salvarsan products an acutely fatal encephalitis with convulsions and coma may ensue in cases of cerebral syphilis. In carbon monoxide poisoning also there may be cerebral lesions involving especially the globus pallidus and areas of demyelinisation of nerve fibres in the white matter.

Lead Encephalopathy may also be grouped in this category, but it is described on page 701.

CHOREA

Under this heading are included two types of disease wholly unrelated in nature and incidence, but alike in that they are characterised by the appearance of involuntary movements, irregular and spasmodic in character, occurring during rest, and also superimposed upon voluntary movements which they render inco-ordinate.

The one is known as rheumatic or Sydenham's chorea, and is an extremely widespread malady of children dependent upon an infective inflammatory lesion of the brain ; the other is a rare chronic, progressive malady of middle-aged or elderly persons, which, when it is associated with mental deterioration, is known as Huntington's chorea, otherwise as chronic progressive chorea. It depends upon degenerative changes in the brain and has been described already (*vide* p. 613).

Rheumatic Chorea (*Sydenham's Chorea*)

Ætiology.—It is a disease of young persons, nearly all cases occurring between the ages of five and twenty years. Girls are affected more frequently than boys in the proportion of three to one, and it is most common amongst children reared under unfavourable hygienic conditions. It is essentially a manifestation of rheumatic infection of the cerebral hemispheres, and the subjects of chorea commonly give a history of other evidences of rheumatic infection : thus a history of acute rheumatism, "growing pains," of sore throat, or sometimes of rheumatic nodules, is obtainable in almost all cases. In a first attack of chorea it is not the rule to find objective evidence of

rheumatic endocarditis, but in second and subsequent attacks signs of cardiac involvement are much more common.

Occasionally rheumatic nodules and fleeting joint pains of mild character may be noted during the course of an attack of chorea.

Predisposing factors in the subjects of the essential infection are a neuropathic inheritance, emotional instability, and debility.

Pathology.—The essential lesion is a disseminated meningo-encephalitis affecting the cerebral cortex, corpus striatum, and pia arachnoid. The organism responsible for the lesion is in all probability the same as that which causes rheumatic carditis and arthritis. On microscopic examination, changes closely resembling those found in lethargic encephalitis are seen.

Symptomatology.—The common mode of onset is subacute, and for one or more weeks before the appearance of the characteristic involuntary movements the child is noticed to be fretful, easily tired, and to be sleeping badly. Then a general motor restlessness is noticed, the child becomes fidgety, clumsy in movements, drops things, and knocks against the furniture in moving through the room. Obvious involuntary movements then appear, the patient grimaces, twists jerkily, shrugging the shoulders and making sudden irregular movements of the head and limbs. These movements are increased in distribution and severity if the child be reprimanded, or has to carry out any purposive movement. Sometimes the articulation becomes disordered. Associated with these symptoms is a generalised muscular weakness, emotional instability, and in severe cases definite mental excitement and derangement.

The involuntary movements are true movements and not simple muscle twitches ; they are rapid and variable in form. If the patient be asked to grasp the examiner's hand it will be noticed that the muscular contraction is irregularly sustained and intermittent in character. In addition, adventitious movements of the arm at elbow and shoulder occur and the limb is jerked irregularly to and fro as the grasp is kept up. Further, the involuntary movements in other parts of the musculature are increased, so that the patient grimaces, and the head and lower limbs go into unceasing movement. The tongue, when protruded, is jerked back rapidly into the mouth, and cannot be withdrawn voluntarily except in jerks. The respiratory muscles partake in the general disturbance, and the rhythm and force of respiration are irregular.

The movements may be predominantly unilateral, but are rarely absolutely so. For example, the facial musculature is always bilaterally affected.

The muscular weakness varies from case to case, and in some instances is the predominating feature of the condition, involuntary movements being minimal. This is the so-called chorea mollis. The child lies limply on its bed, the musculature is profoundly flaccid, and all movements are performed feebly and readily cause fatigue. The reflexes are not qualitatively altered, though in the flaccid cases the tendon jerks may be diminished, or even lost. In some cases a peculiar phenomenon is seen on eliciting the knee jerk with the leg slightly flexed. The leg rises from the bed and remains suspended in the air for a second or so before flopping back on to the bed, owing to the imposition of a choreic upon the reflex movement. The abdominal reflexes are retained and the plantar responses are of normal type.

Although in first attacks of chorea definite evidence of rheumatic affection of the heart is frequently absent, yet slight dilatation and rapidity of the heart are common. In recurrent attacks endocarditis is often found.

In a large number of subjects, second and third attacks occur at intervals of several months.

Chorea may be met with in young women during their first pregnancy, the symptoms developing during the first three months and often becoming extremely severe. Added to a continual motor restlessness there may be active delirium and considerable weakness. Death may occur from exhaustion. It may recur in subsequent pregnancies.

Course.—The duration of a case of average severity ranges from six weeks to several months. The longer course is seen in the absence of adequate measures of treatment and management. Sometimes temporary improvement or apparent recovery may be followed by recurrences, and thus the disease spreads out over a long period. Death from exhaustion occurs in a small number of cases, usually when the patient is adolescent or a pregnant woman. Rheumatic heart disease may also be responsible for a fatal issue.

Diagnosis.—The two maladies with which Sydenham's chorea are most likely to be mistaken are multiple tics and the choreiform type of lethargic encephalitis. In the former case, the involuntary movements tend to be repetitive and peculiar to any given case, and cease in an affected limb when this is in voluntary use. There is no dysarthria, nor does the subject drop objects from the hands. The tic-like movements may persist for years or may suddenly change in form. In lethargic encephalitis the onset of choreiform movements is usually sudden, and there are associated ocular palsies: ptosis, squint, and diplopia. Slight fever, disturbances of sleep, and nocturnal delirium may also occur.

Treatment.—In cases of recent onset and of all grades of severity, rest in bed under conditions of reasonable quiet is essential. The period of rest varies with the severity and with the rapidity of response to treatment. Separation from other children is advisable, but it is necessary to keep the patient contented and quietly amused. Since the subjects of chorea are frequently debilitated and badly nourished, their feeding must be carefully attended to. In profoundly restless cases nasal feeding may be necessary, and in these circumstances particular efforts must be made to maintain nutrition as far as possible. When the movements are violent, the patient must be protected from injury by pillows arranged round the bed and by cotton wool and bandages round the limbs.

In the matter of drugs, aspirin is the most useful agent and is well tolerated by patients with chorea. For children from five to fifteen years of age 10 gr. three or four times daily may be given, and 15 gr. for older patients. If this does not suffice to procure sleep, luminal or chloral and bromide may be given at night. In severe or resistant cases, the addition of chloretone (5 gr. twice daily for a child of ten, and for a limited time) may be beneficial, but it should not be used as a substitute for aspirin.

During convalescence general tonic treatment is indicated. Cod-liver oil and malt, iron, and arsenic may all be usefully employed.

DISSEMINATED SCLEROSIS

Clinically, disseminated sclerosis is a malady of otherwise healthy young adults, usually characterised by an intermittent course which depends upon the acute development at irregular intervals and in various parts of the brain

and spinal cord of multiple inflammatory foci. These lesions give rise to acute outbreaks of symptoms with intervals of improvement and quiescence.

Ætiology.—Nothing certain is known of the causative agent in this disease. The fresh lesions are undoubtedly inflammatory in nature, but whether an organism or a circulating poison is responsible is unknown. It is essentially a malady of early adult life, its onset being rare before sixteen years of age or after forty-five. Females are more frequently affected than males, in the proportions of five to two. It is found with equal frequency in urban and rural dwellers and in persons of all social grades and modes of life. In this country it is now the commonest organic nervous disease, exceeding neurosyphilis, and is still increasing in frequency. Various factors have been invoked as either causative or precipitating, but with no convincing evidence. Thus, it may first become apparent after pregnancy and parturition, after trauma or after infectious illnesses, but some at least of its principal symptoms are so insidious in onset that these alleged relationships can never be established satisfactorily.

Morbid Anatomy.—The primary lesion is one of medullated nerve sheaths within the brain and spinal cord, with associated secondary neuroglial and vascular reactions. The foci of the disease are scattered thickly throughout the nervous system, being usually most abundant immediately beneath the cerebral cortex and beneath the ependymal lining of the ventricles, and spread at random throughout all parts of the brain stem and cord. The cerebellum is less thickly sown with patches of disease than the rest of the nervous system. The lesions vary in size from microscopic foci to patches of one or more centimetres in diameter. They are sharply delimited from normal tissue and are wholly irregular in outline, invading grey and white matter indifferently.

The optic nerve is very commonly the seat of one or more lesions. The myelin sheaths are early destroyed and the axis cylinders stripped. The former degenerate into fatty droplets and the latter may be distorted. Neuroglial reaction is present, and varies in appearance and intensity according to the age of the lesion. Nerve cell bodies included within a patch undergo some chromatolysis, but are much less severely affected than the nerve fibres. To the naked eye a fresh patch has a pinkish, swollen, translucent appearance, but old patches are grey and sclerosed.

Symptomatology.—The clinical course of the disease may usefully be divided into two stages: the stage of evolution and the stage of full development.

The stage of evolution may be long drawn out, and it may be ten or more years before the malady is fully developed. The initial symptoms are of two orders: those referable to lesions of the spinal cord and those due to lesions in the brain stem and optic nerves. The spinal cord symptoms are usually very slow and insidious in onset, and have been present in most cases for one or more years before the subject seeks medical advice. They consist in a slowly developing weakness of one or both legs, which is first manifested as undue fatigue on walking and then by actual dragging of the foot or feet when the subject is tired. This slow progress may be interrupted by a sudden marked exacerbation of weakness in one leg, which makes unassisted walking impossible for a week or more, and then slowly clears up, leaving a variable degree of residual weakness behind. It is not uncommon for the initial symptoms to be regarded by the patient as due to some local disorder of the leg

or foot, such as " rheumatism," " sprain," or " displaced cartilage of the knee " until after a year or more the increasing severity of the disability leads the doctor to question the patient's diagnosis, and for the first time to make an adequate clinical examination.

The upper limbs are peculiarly prone to sudden temporary accesses of what the patient describes as " uselessness," which are found on examination to consist of severe ataxy due to impairment of the sense of position and rarely to true motor weakness.

Punctuating this course of events, or even preceding it by one or more years, there occur striking symptoms of acute onset referable to the optic or oculomotor functions. Transient blindness or severe impairment of vision in one eye, of rapid onset, of one or two weeks' duration, and followed by complete or almost complete restoration of vision, or transient diplopia without unequivocal squint are the characteristic expression of these lesions. This impairment of visual acuity is the result of retrobulbar neuritis (*vide* p. 658). At the time when the disturbance is first noted ophthalmoscopic examination is negative, though rarely a slight œdema of the optic disc may be noted. The temporal pallor which ensues is not present for some weeks later. These may recur at intervals, affecting first one eye and then its fellow. At this stage of the disease, nystagmus, scanning speech, and intention tremor are quite exceptional, except in those few cases in which the cerebellar projection fibres in the brain stem are involved early and severely. These three symptoms, the so-called triad of Charcot, are commonly symptoms of the fully developed disease, and are not constant even then. They are not essential to a diagnosis of the disease, and if they are so regarded its recognition must always be unwarrantably delayed. Fleeting pains of moderate degree in back and limbs and paræsthesiæ in the extremities are common. Some cases develop rather rapidly with the simultaneous appearance of weakness and paræsthesiæ in one or more limbs, while a fulminating onset with intense vertigo, sickness, and inco-ordination may also be met with.

During the years that this slow and variable progress of the disease goes on the patient may have intervals of several years of apparently quite perfect recovery, in which even objective physical signs may be difficult to find. The fugitive character of signs and symptoms has given rise to the view that hysterical phenomena are common concomitants of early disseminated sclerosis, and many early cases of the malady are regarded as hysteria when a careful history is not taken and no opportunity occurs of examining the patient during the transient presence of the disabilities complained of. The slight emotional facility which many patients show is an added basis for this belief. In exceptional cases no remissions occur.

Examination during the stage of evolution reveals in most cases an absolutely typical group of physical signs. The tendon reflexes are exaggerated, and there may be unilateral or bilateral ankle clonus, the plantar responses are of the extensor or Babinski type on both sides, the abdominal reflexes are commonly absent, and the legs may show a minimal degree of spastic paresis. Although the disability of the limbs complained of may be one-sided, examination commonly reveals bilateral physical signs. In addition, there may be pathological pallor of the temporal halves of one or both optic discs and a loss of vibration sensation in the legs. This group of signs, in the absence of cutaneous sensory loss, is an adequate basis for the diagnosis of the disease. Other signs may sometimes be added to these, including

nystagmus, slight intention tremor of the hands, and some ataxy of gait (due to impairment of the sense of position in the legs).

In *the stage of full development*, which, happily, some patients never reach, there is definite spastic paresis of the legs, and the patient may be bedridden or require assistance in walking. Flexor spasms in the legs have begun to occur, and precipitancy and even incontinence of urine. The arms may be ataxic or show that form of unsteadiness on purposive movement known as intention tremor. Nystagmus and a peculiar spacing of syllables in articulation may be present. By this time there is a severe degree of permanent unvarying disability, and remissions of any great degree have ceased to occur. Finally, after a varying period of years, flexion contracture develops in the legs, with profound loss of voluntary power, the sphincters act involuntarily, the arms are unsteady, the articulation grossly disordered, and tremor of the head and trunk may accompany all attempts at movement. In addition, the patient is very euphoric and fatuous, having little insight into the severity and hopeless nature of his condition. Occasionally gross symptoms of mental disorder of variable character may be present. Death ensues from some intercurrent infection, pulmonary or urinary, or by septic absorption from bed-sores.

In some cases the progress of the disease is indefinitely arrested in the earlier stages, and the patient continues to lead a restricted life for many years.

Characteristic of the malady in most instances is the absence or late appearance of cutaneous sensory loss. Loss of the sense of position in the limbs and of vibration sensation is common.

The blindness which may occur as an incident in the disease is never permanent, though an attack of retrobulbar neuritis from development of a patch of disease in the optic nerve may leave some degree of visual impairment and a marked degree of pallor of the discs. Permanent paresis of cranial nerves is also exceptional.

Cerebrospinal Fluid.—In about 50 per cent. of cases there is a slight mononuclear lymphocytosis, little or no protein increase, a negative Wassermann reaction, and a "paretic" type of Lange colloidal gold curve. For further details on the last-named reaction the reader is referred to page 636.

Diagnosis.—Although it may be difficult, an accurate diagnosis can usually be made even in the earliest stages of the malady. The typical combination of history and signs are not found in any other malady. The gravest difficulties arise in those cases where transient blindness precedes all other signs and symptoms. The patient is usually a young woman in whom, during the course of a few days, vision has rapidly failed in one eye, being reduced to appreciation of hand movements. Examination of the fundus oculi reveals nothing whatever abnormal until several weeks have elapsed and after visual acuity has been restored. Despite the extreme rarity of retrobulbar neuritis from sphenoidal sinus infection and its extreme frequency in disseminated sclerosis, a diagnosis of sinus infection is often made in cases of the kind, and the inevitable restoration of vision is attributed to whatever operative procedures may have been adopted to drain the sinus. The patient at the time may present no objective signs of any nervous system disease.

Another fruitful source of error is provided by cases in which the signs and symptoms suggest a focal lesion of the spinal cord, with cutaneous sensory loss up to a segmental level. In these cases the presence of exaggerated

tendon reflexes in the arms, of pallor of the discs, of slight nystagmus, and of an indistinctness or variability in the upper level of sensory loss should always give rise to suspicion as to the true nature of the condition present. Further, examination of the cerebrospinal fluid may serve to differentiate compression of the cord from disseminated sclerosis, in which disease the fluid may be normal in the early stages or present no other abnormality than a slight lymphocytosis and slight increase of protein, and is always colourless and clear.

In other cases again, ataxic symptoms and disturbances of ocular movement may precede definite indications of pyramidal tract involvement, and a diagnosis of focal pontine or brain stem lesion may be made. In the great majority of cases, however, the combination of signs given above as characteristic of the stage of evolution is present and makes a correct diagnosis possible.

Prognosis.—Although disseminated sclerosis is a progressive malady ending in most cases—though not in all—in profound disability, yet nothing can be more difficult than to give a prognosis in an early case. This is especially so when we remember that retrobulbar neuritis is commonly an initial symptom, occurring sometimes years before any other manifestation of the disease develops. In other words, a young person with a unilateral retrobulbar neuritis may have an unknown period of normal health before her, ranging from weeks to years. In such circumstances the greatest caution in giving a prognosis to the patient or her relatives should be observed, and rash generalisations as to the advisability of marriage, for example, should, out of ordinary humanity, be avoided and not offered uninvited.

Once symptoms referable to a spinal cord affection have made their appearance a graver prognosis as to the possible duration of wage-earning capacity is justifiable, though even here long remissions are not rare and the future depends in some degree on the nature of the patient's work : hard physical work being more likely to have adverse results than purely sedentary work. Very many subjects of disseminated sclerosis do in fact remain at work for years after the nature of their illness is declared. Perhaps there is no malady in which the future of the individual patient is more difficult to forecast, and no situation in which an economy of speculation is more expedient.

Treatment.—There is, unfortunately, no method of treatment which is certainly known to influence the course of the malady, and this course is so capricious and the occurrence of long remissions so common that the assessment of any mode of treatment is extremely difficult. In the circumstances it is not surprising that extravagant claims are made from time to time in favour of this or that mode of treatment by those not familiar with the natural history of the disease.

Amongst recent methods for which favourable results have been claimed are protein shock therapy, pyrotherapy, electrotherapy, and liver treatment. In respect of none of these is there available any sound evidence of their efficacy.

It has long been known that fever occurring during the course of disseminated sclerosis affects it adversely, and it is not clear that artificially produced fever is free from the same danger.

It cannot be said that the traditional practice of giving arsenic (either by mouth or by the injection of organic compounds) has ever justified its use, and the same may be said of the other anti-syphilitic drugs which have been employed.

Recently, the use of quinine (quinine bihydrochloride 5 gr. twice daily) has been advocated. Here, again, the proof of its value is yet to be established, but the drug produces no harmful reactions and it is worthy of trial.

Perhaps more important than any formal method of treatment is the right ordering of the patient's life when this is practicable. All forms of fatigue must be carefully avoided, and their inadvertent occurrence must be dealt with by corresponding rest. Infectious illnesses, trauma, and other forms of stress all have a deleterious influence on the course of the malady. Although it is not usual for the symptoms to increase should pregnancy supervene in the patient, yet delivery is often followed by an exacerbation of the malady, which may even first come to notice in these circumstances. The presence of disseminated sclerosis is not in itself an indication for any intervention in the course of a normal pregnancy, but only for greater care of the patient during this period. Indeed, the artificial termination of pregnancy is sometimes as disastrous as a full-term confinement. Should an outbreak of symptoms occur, the patient is best kept in bed for two or three weeks, with massage to maintain the muscular condition. While any obvious focus of gross infection may usefully be dealt with as an adjuvant to treatment, it is unwise to expect such measures to have any material influence on the course of the disease, and indeed meddlesome therapy of this order may even be harmful in the reactions it provokes.

ACUTE DISSEMINATED ENCEPHALOMYELITIS AND NEUROMYELITIS OPTICA

The relation of these two maladies to each other and of each of them to disseminated sclerosis is not yet certain. All three are essentially demyelinating diseases, but those two now under consideration are more acute and severe in the lesions associated with them.

In the brain the lesions are mainly confined to white matter. They are small and multiple. Not only may the myelin sheaths be destroyed, but the axis cylinders also, while there may also be glial cell degeneration and tiny areas of softening and even of cavitation. In neuromyelitis optica or Devic's disease, as it is also called, the optic nerve is similarly affected. These maladies occur at all age periods.

Neuromyelitis Optica.—The symptoms are those of a transverse myelitis of rapid onset and of a retrobulbar neuritis (central scotoma, and even complete blindness, œdema of the optic discs). The myelitis may precede or may follow the retrobulbar neuritis, and an interval of months may separate them. The paraplegia is often total, and may ascend for a time, so that respiratory failure and death may ensue. On the other hand, recovery may occur. Vision may be almost completely restored, but some defect commonly remains, and after the lapse of some months the characteristic pallor of primary atrophy appears.

The cerebrospinal fluid may show an increase of lymphocytes (up to 50 to the cubic centimetre).

Treatment has no influence upon the disease process, and the care of the patient is that of any case of paraplegia.

Acute Disseminated Encephalomyelitis.—The symptoms may be those of an acute and severe disseminated sclerosis. There are headache, sickness, and

vertigo, sometimes stupor or delirium. There may be weakness and unsteadiness of the limbs, with the reflex changes characteristic of pyramidal lesions. Recovery or death may ensue.

As for neuromyelitis optica, there is no specific treatment.

THE VIRUS DISEASES OF THE NERVOUS SYSTEM

(*Poliomyelitis, Encephalitis, Herpes Zoster, Rabies*)

Under the heading of Virus Diseases we must include poliomyelitis. epidemic encephalitis, the encephalitis and myelitis that may follow vaccinia and the acute specific fevers, rabies, and also herpes zoster.

Owing to their affinity for the nervous system the viruses in question are known as neurotropic, and since they act primarily upon the nerve cell they are also spoken of as polioclastic. They multiply and exert their pathogenic activity only in contact with the living cell, within which their life and activity are short-lived. After a short period they disappear, and thus virus diseases are said to be self-limiting. By the term "neurotropic" we imply a virus that attacks the nervous tissues, either nerve or glial cells or both. directly and primarily. The virus of poliomyelitis attacks only the former, that is, the nerve cell, and is thus spoken of as neuronotropic. As far as we know viruses do not attack white matter.

In all cases the virus is to be found in the nervous system and not in the blood and cerebrospinal fluid, and the virus infections are looked upon as primary in the nervous system and not as secondary to generalised, systemic infections.

POLIOMYELITIS (*Infantile Paralysis*)

Ætiology.—The responsible organism is one of the smallest filterable viruses known. Man and the chimpanzee are the only natural hosts, though other monkeys can be successfully inoculated. Under experimental conditions the disease can be conveyed by inoculation through the cerebral, intranasal, tonsillo-pharyngeal, vitreous, and intestinal routes, the tonsillo-pharyngeal being the most uniformly successful. This fact is significant when we recall that cases of the bulbar type of poliomyelitis may occur, during epidemics of the disease, in children subjected to tonsillectomy or adenoidectomy.

The view formerly held that the habitual portal of entry of the virus into the nervous system in man was the olfactory one, namely, from the nasal cavity via the filaments of the olfactory nerves into the brain, has lost ground since recent histological investigations have failed to find the characteristic tissue reaction to the entry of the virus in the olfactory bulbs or tracts. Further, the presence of virus in the stools in human cases and in the gut wall in the experimental disease has led to the suggestion that the alimentary tract may provide the common port of entry: the pharynx in bulbar and the bowel in spinal cases. It is suggested that the virus passes thence by sympathetic nerves into the spinal cord.

Further, since the virus can, by means of monkey inoculation experiments, be detected in the stools not only during the acute illness but also for some weeks afterwards, the belief that chronic carriers do not occur in the case of

poliomyelitis appears to be invalid. Unfortunately, no ready means of detecting carriers exists, for there are no specific precipitin, complement-fixation, or cutaneous tests for poliomyelitis.

There is no conclusive evidence that the virus can infect or multiply in extraneural tissues, and therefore the present view that poliomyelitis is an exclusively nervous system infection still holds.

The *incubation period* is believed to be from five to twelve days.

Epidemiology.—The view that poliomyelitis is an exclusively human-borne disease is at present undergoing modification, for the virus has been found in active form in the bodies of flies frequenting localities where the disease is present and these insects may therefore act as vectors, though the evidence is far from conclusive. In its epidemic form poliomyelitis is usually a malady of the autumn, and epidemics tend to die down rapidly when the weather turns cold and frosts appear: that is. when house flies disappear. It has also been suggested that milk may be a vehicle of infection. Other modes of spread may depend upon the fact that the virus is active in the fæces of sufferers and of convalescents, and has been isolated from sewage coming from a focus of infection.

Two types of individual carry and spread the infection, the healthy carrier of the virus and patients suffering from the disease in its non-paralytic form and in the pre-paralytic stages. Even paralysed patients during the first two weeks of the illness may be infectious, though once paralysed their opportunities of spreading the malady are restricted.

It is probable that the infectivity of the disease varies from epidemic to epidemic, and there seems to be a high degree of natural resistance in the community. This may in part be an acquired immunity on the part of individuals who in infancy have suffered from an unrecognised abortive attack of the disease. A single attack gives permanent immunity to the individual. Protective antibodies have been found in adult human serum in 70 per cent. of all sera tested, though whether this depends upon a prior, non-paralytic attack of the disease or not is not certain. In assessing the value of official notification figures of cases of poliomyelitis during epidemic prevalence, it is well to remember that diagnosis in the pre-paralytic stage, or in the non-paralytic form of the malady, is not always easy, and many cases are notified that prove subsequently not to be cases of this disease. This is probably true of as high a proportion of total notifications as 60 per cent. When it is also borne in mind that the ratio of non-paralysed to paralysed cases may be of the order of 4 to 1, it will be seen that during the course of an epidemic outbreak alarmist views as to its severity readily gain ground.

Pathology.—The primary and essential lesion of the disease is in the nerve cell, and the virus appears to have a special affinity for the large cells of the ventral horns of the spinal cord, especially in the lumbar region. The lesions vary from chromatolysis to complete necrosis. Immediately following this, an inflammatory reaction with exudate appears in the interstitial tissue of the neighbouring grey matter, in the perivascular spaces, and in the meninges. This reaction in turn leads to alterations in the cerebrospinal fluid. It was formerly thought that this reaction and the resulting change in the fluid were all precursors of the cell lesion, but it is now known that they are consequences of the latter. Although the nerve cell lesions which lead to paralysis are those in the brain stem and spinal cord, an encephalitis is an essential

element in every case of the disease, even in those in which paralysis does not ensue. The virus and the reaction it produces are invariably present in the motor cortex, thalamus, vestibular and cerebellar nuclei, but the lesions it produces there are not such as to lead to paralytic manifestations: for example, there is no conclusive evidence that there is a cerebral or upper motor neurone type of paralysis in poliomyelitis, though the contrary is commonly stated. In the monkey, for example, this type of paralysis cannot be produced even when the virus is inoculated directly into the cerebral cortex, and in these circumstances only a lower motor neurone paralysis (brain stem or spinal cord) ensues.

The distribution of virus and of lesions constant in every fatal case is in the motor region of the cerebral cortex, the subthalamus, the cerebellar and vestibular nuclei, the grey matter of the brain stem and the ventral horns of the spinal cord.

Symptoms.—It is necessary to preface what is to be said under this heading by stating that three grades of severity of infection must probably be recognised in this malady: a *subclinical* infection, that is, one without clinical manifestations but with characteristic changes in the cerebrospinal fluid; a *non-paralytic infection* in which there are both characteristic clinical symptoms together with cerebrospinal fluid changes, constituting an illness of but a few days' duration followed by recovery with no residual symptoms; and a *paralytic infection*, differing from the non-paralytic in that the intensity of pathological change in motor nerve cells in brain stem or in cord, or in both, has been sufficient to lead to paralyses.

It has hitherto been the custom to speak of the non-paralysed case as being an "abortive" case of poliomyelitis, but this is misleading in that in both "types" lesions are found in the nervous system of the same general distribution, the essential difference being one of intensity of change in affected nerve cells. The term "abortive" will not be used, therefore, in this account, and it should be generally abandoned.

It remains, further, to be said that in paralysed cases the onset of paralysis is preceded by the same symptom-complex as makes up the non-paralysed case, but in the paralysed case we speak of it as constituting the *pre-paralytic phase* of the illness.

For purposes of description it is useful, perhaps, to divide the pre-paralytic phase into two stages: an initial phase in which the child, or older patient, complains of headache and malaise, but of no other constant symptoms. Within a few hours the temperature rises to 101° to 103° F. and the second phase opens with increase of headache, stiffness of neck and back, and perhaps pain in both. The patient may vomit once or twice, loses appetite, and commonly sweats freely over a period of twenty-four to thirty-six hours.

Signs of meningeal irritation now become plainly visible; stiffness of neck and back, Kernig's sign, an inability of the patient to flex neck, back, and leg sufficiently to be able to touch his knee with his nose. The temperature remains raised, the child becomes silent or fretful, sleeps badly, and becomes constipated. Drowsiness is a less common symptom. A curious weakness of the sternomastoid muscles may now be noted, so that the patient cannot lift the head against any resistance. Local muscular twitchings may be noted. The tongue is commonly coated. Herpes labialis, so common in cerebrospinal fever, is not seen save rarely.

It is sometimes possible to surmise which patients are going to be severely paralysed, for these look more prostrated and ill and heavy-eyed.

Having reached its fastigium in some forty-eight to sixty hours, this febrile illness may rapidly clear up and recovery ensue, or within a few hours the temperature may again rise and paralyses make their appearance. Again, paralyses may develop without any intervening afebrile period.

In the sporadic case paralysis is generally maximal at onset, but during epidemic outbreaks this is less commonly the case, and then paralysis may spread and deepen in sudden exacerbations at intervals of some hours for two or three days, when a final drop of temperature to normal occurs and no further extension of paralysis develops.

It has long been known that in epidemics of the disease a proportion of patients make a recovery before the appearance of the third stage. These are the non-paralysed cases. In these the virus has been neutralised by the natural resisting agencies in the body before it has been able to damage the nerve cells sufficiently to produce paralysis. It is not correct to regard them as cases in which the virus has not succeeded in gaining access to the nervous system. It is believed that as many as 70 per cent. of all infected children during an epidemic may escape paralysis in this way.

It has in the past been customary to speak of cerebral, cerebellar, brain stem, spinal and neuritic types of poliomyelitis, but it is highly probable that all but the brain stem and spinal forms of paralysis are not due to infection by the virus of poliomyelitis, but constitute a mixed group of infections of varied and unknown origin. We shall therefore only consider brain stem and spinal paralyses.

The paralysis may vary from weakness of a single muscle to widespread paralysis of limb and trunk musculature. When the paralysis is limited in extent, the deltoid and the dorsiflexors of the foot and toes are especially prone to be picked out, but there may be extensive paralysis of one or more limbs, with or without involvement of abdominal, back, neck, and thoracic muscles. As a rule the paralysis is maximal in degree and extent at the moment of onset, but an ascending paralysis, or the spread at short intervals of paralysis from limb to limb, may occur. Ascending paralysis terminating in involvement of the respiratory muscles and death within a period of hours is more common in cases occurring during epidemics, especially in adult patients. Of the total number of muscles involved, some are totally paralysed and a greater number weakened. In a few cases there is a widespread slight paresis of muscles, which is apt to be regarded as a general debility following the febrile constitutional disturbance which precedes it. Similarly, cases in which paralysis or paresis is restricted to the back or abdominal musculature may escape diagnosis. For a period varying from one to several weeks some or all of the affected muscles may be painful and extremely tender on manipulation. When these symptoms pass off the patient is said to have entered the convalescent stage of the disease.

Wherever there is an appreciable weakness of a muscle the corresponding tendon jerk is greatly diminished or abolished. Sensory loss does not occur, and the only sphincter disturbance is a temporary retention of urine which rarely lasts for more than two or three days.

When the period of convalescence is entered, the affected muscles may be divided into those which recover rapidly and completely, those which make a gradual and partial recovery, and those which remain permanently paralysed.

The last two groups undergo progressive wasting, and in severe cases extreme and widespread muscular atrophy may ensue, with defective growth of the affected limbs subsequently. Under adequate treatment some degree of progressive improvement may go on for two or even three years. After this period no further improvement can be expected.

In the process of wasting, fibrous tissue forms in the muscles, and unless appropriate measures are taken from the outset may result in considerable deformity of the affected region.

The Cerebrospinal Fluid.—The examination of this fluid is of great importance if a diagnosis is to be made during the pre-paralytic stage of the disease. The fluid may be normal during the opening hours of the first phase, but as the second phase is reached the cellular content rapidly increases. At first polymorphonuclear cells predominate (from 30 to 150 per c.mm.), and when the count is high the fluid may be opalescent. Very soon the proportion of lymphocytes increases, and towards the end of the febrile period they outnumber the polynuclear cells. The globulin content of the fluid is raised, but the chlorides and glucose remain unchanged, thus differentiating the cerebrospinal fluid changes from those of acute meningitis. After the appearance of paralysis the cellular increase drops rapidly, but the protein content may remain high for two or three weeks.

These changes in the fluid were formerly thought to express the invasion of the subarachnoid space by the virus, and to precede the invasion of the nervous tissues. It is now known, however, that they follow and are a consequence of the pathogenic activity of the virus within the nerve cells. It is important to recall here that these changes in the cerebrospinal fluid are essentially those regarded as characteristic of what is called acute aseptic, or benign lymphocytic, meningitis, and further to remember that the symptoms of the pre-paralytic stage of poliomyelitis are, in form and duration, those of this variety of meningitis. We have not until recently been in the habit, in this country, of diagnosing non-paralytic cases of poliomyelitis, though such cases must undoubtedly occur from time to time ; and it is highly probable that a proportion of cases thought to be benign lymphocytic meningitis are in fact non-paralytic cases of poliomyelitis.

Diagnosis.—Experience in the recent outbreak in this country has shown how difficult it is to recognise this malady in its pre-paralytic phase or its non-paralysed forms. Cases of cerebrospinal fever, infective mononucleosis, enteric, follicular tonsillitis, osteomyelitis, and indeed of every febrile ailment, find their way into reception wards after notification as acute poliomyelitis.

It is probable that, assuming careful clinical examination, the only real difficulty lies in the differentiation, in their initial phases, of cerebrospinal fever and poliomyelitis. In both there are signs of meningeal irritation with fever, but within a few days they differentiate themselves clinically. However, owing to the great importance of instituting chemotherapy in cerebrospinal fever at the earliest possible moment, it may be necessary to examine the cerebrospinal fluid. Here the findings are essentially different, the cellular increase in poliomyelitis being usually predominantly lymphocytic as opposed to cerebrospinal fever where it is polynuclear. In poliomyelitis chloride and glucose levels remain normal, in meningitis both fall notably. In poliomyelitis, finally, no organisms are seen in the fluid, which remains clear, or almost clear, and is non-purulent.

Treatment.—This includes (i) measures intended to cut short infection before the nerve cells have been irreparably damaged, (ii) measures to prevent the spread of infection to susceptible persons, and (iii) measures for dealing with paralysis when this ensues.

It has long been known that the serum of persons who have survived an attack of poliomyelitis, so-called convalescent serum, has the power of protecting that susceptible animal, the monkey, from infection under certain conditions. These conditions are that serum and infective material are inoculated together into the animal, or that the serum is given not later than twenty-four hours after inoculation with infective material. On the other hand, if any symptoms of poliomyelitis have appeared in an infected animal it is then useless to give serum, since it neither cuts short nor mitigates the severity of the disease. It need not surprise us, therefore, that this mode of treatment has proved valueless in the human disease.

So far we have no known method of cutting short the infection, or of preventing the development of, or controlling the extent and severity of, paralysis. For the first few days of the illness the nasopharyngeal secretions, and, for a longer and as yet undetermined period, the fæces are infective, and this fact should be borne in mind in the management and nursing of the patient which should follow, in respect of infectivity, the general lines adopted in a case of typhoid. Further precautions to lessen the possibility of spread have been suggested in the United States, *e.g.*, that contacts should not handle food for distribution for at least a fortnight, and that no nurse younger than twenty-five years should nurse a case. It has to be admitted, however, that case to case infection is not often to be traced, though authentic examples are on record. Tonsillectomy and adenoidectomy should not be performed on children during the presence of an outbreak of poliomyelitis, as there is a liability to infection, with the development of the bulbar type of paralysis, through the lesion in the fauces and nasopharynx. The sulphonamide drugs and penicillin are of no value whatever, as far as present evidence indicates, in the treatment of poliomyelitis at any stage, except for the prevention and treatment of respiratory or other infections.

The only indication for drugs is muscular pain, and for this purpose acetyl-salicylic acid is generally adequate.

The most arduous part of treatment is that of the paralysed muscles. To be effective it must be continued in severely paralysed cases for a very long period, and some general principles only can be formulated here. The three essentials are muscular rest, the maintenance of good posture, and re-education exercises. While pain persists, massage and electrical stimulation are contraindicated, but gentle passive movements at all joints and light splinting of dropped feet are indicated from the outset. From the moment that paralysis develops, the affected muscles must be kept at rest in a position of relaxation. The legs must be extended, adducted, and rotated in so that the feet lie side by side. Similarly, the hand should be kept in the mid-position, and the shoulder abducted when the deltoid is affected. If the erector spinæ (sacrospinalis) be involved, the patient must be kept in the supine position for several weeks and not allowed to sit up until a mechanical support has been prepared.

As soon as possible, when suitable mechanical support has been provided, the patient should be got on his feet whenever feasible. Re-education exercises now become of value. These consist in assisted active movements

of the weakened muscles, in which the movement is attempted with the muscle almost in the position of greatest shortening ; that is to say, a full excursion of the limb is not attempted. By varying the patient's position and by giving active help the weight of the limb is taken off the muscle, and the action of gravity overcome. Such movement should be undertaken daily for short periods, fatigue being carefully avoided. With returning power less active assistance is required. Walking exercise with a walking chair must be employed when possible.

Massage takes secondary place in treatment, and is most useful for those muscles which, being totally paralysed, cannot be dealt with in any other way. It must never be regarded as an adequate substitute for active exercises. Despite a widespread belief to the contrary, there is no unequivocal evidence that any form of electrical stimulation is of the slightest use in assisting in the recovery of power in paralysed or weakened muscles, and its employment is harmful if it replaces rational and useful modes of treatment.

When, during the acute stage, paralysis invades the respiratory muscles death may ensue from asphyxia. To tide the patient over this peril the use of respirators has been adopted. The box respirator of the Drinker type is the most effective. In this the patient is enclosed, his head protruding at one end of the box through a rubber collar round the neck. A motor produces rhythmic positive and negative pressures within the respirator and the chest is passively moved. For cases in which the main lesions are bulbar, and respiratory difficulty arises from involvement of the respiratory centre, their use is strongly contraindicated, and the careful clearing of the air passages from accumulating secretions is essential.

The outbreak of an epidemic of poliomyelitis in a school presents problems of some difficulty. Clearly, the closing of a day school is imperative, but it has been urged that this step in the case of a boarding school necessitates the dissemination of a number of possible carriers and incubating cases, and may thus lead to further spread of the disease.

On the other hand, the occurrence of case to case infection is established beyond reasonable doubt, and within the school community fresh cases may continue to break out for several weeks. In other words, every healthy child retained within such an infected community remains exposed to infection with its frequently disastrous consequences. There can be no justification for exposing a number of children to this danger. The safest plan, therefore, is probably the disbandment of the school and the segregation of exposed children within their own homes for a period of two weeks, care being taken not to allow them to come in contact with other children in the household.

LETHARGIC ENCEPHALITIS (*Epidemic Encephalitis*)

This malady occurs sporadically and in epidemics, but evidence of the infectivity of cases is uncertain and its mode of spread is unknown. No age is exempt from susceptibility to the disease. During the many years which have elapsed since its recognition the clinical picture of the malady has varied considerably in different outbreaks and has not always conformed to that by which it was originally identified.

Ætiology.—The disease is believed to be due to infection by a specific virus, which so far has been neither observed nor cultivated *in vitro*. It is not

yet certainly established that the disease can be transmitted to animals by the inoculation of brain substance from fatal human cases.

Morbid Anatomy.—Multiple small meningeal hæmorrhages are sometimes seen over the cerebral hemispheres. Microscopically, a widespread inflammatory reaction and extensive neuronal degeneration are found. In rapidly fatal cases the former may be slight, but in cases of longer standing it dominates the histological picture. Although diffuse, these changes tend to be most profound in the region of the basal ganglia and brain stem.

The inflammatory reaction consists in congestion of blood vessels of all sizes, of minute hæmorrhages scattered throughout the brain substance, and of the characteristic perivascular infiltration by lymphocytes and by plasma cells. Numerous lipoid granules, the products of nerve cell degeneration, are also seen in the perivascular spaces.

The cerebrospinal fluid may be normal, but when altered shows a lymphocytosis with normal protein and glucose contents. Up to one hundred cells per cubic millimetre may be present.

Symptoms.—The great number of symptoms and the various combinations and sequences in which they may occur make a clinical description of the malady somewhat difficult. We may divide them into constitutional and nervous symptoms, still further subdividing the latter according to their nature and localising significance.

The constitutional symptoms vary greatly in severity and duration. They may be so trivial as to escape notice, or so profound as to induce a typhoid state, ending in death after some weeks. In its commoner and mild form this phase of the malady consists in a febrile illness of some few days' duration, the symptoms being headache, malaise, minor gastro-intestinal symptoms (of which constipation is one of the most common), pains in back and limbs, and occasionally an erythematous rash. A diagnosis of influenza is often made when such a patient seeks medical advice.

Certain characteristic symptoms, however, should lead to the recognition of the real nature of the illness. These are drowsiness by day, giving place at night to a muttering occupational delirium, and signs of cranial nerve involvement such as squint, diplopia, ptosis, and nystagmus, all of which may be very transient.

The nervous symptoms may be referable to involvement of any part of the nervous system including nerve roots, and they may for practical purposes be divided into irritative and paralytic symptoms. The former include wild choreiform movements with active delirum, Jacksonian convulsions, rhythmic twitching of strands of muscle fibres occurring at random throughout the skeletal musculature, and root pains of extreme severity. The paralytic symptoms are on the whole less diverse, and consist generally of the cranial nerve palsies mentioned above. Paralysis of trunk and limb musculature is rare, but hemiplegia is not unknown.

The characteristic lethargy of the malady is seen in patients in whom paralytic symptoms occur, and is commonly absent when irritative symptoms predominate. The lethargic patient lies apparently asleep, but is readily aroused to answer simple questions, relapsing at once into lethargy unless his attention is continually held. At night he tends to emerge from this state, passing into the occupational delirium already mentioned.

Many of the milder cases remain ambulant throughout the illness, the

occurrence of which is first recognised, sometimes months later, by the development of characteristic sequels of the disease.

It is clear that the physical signs found on examination vary greatly from case to case, but their general character will be evident from what has been said. Thus the combination of lethargy, ptosis, squint, and diplopia, with a mild febrile reaction, is perhaps the commonest clinical expression of the disease. The reflexes present no characteristic changes and vary from case to case. Sensory loss is exceptional. It is doubtful if fresh cases of this malady have occurred in this country for some years, and cases so diagnosed not rarely prove to be tuberculous meningitis or cerebral tumour.

Course and Prognosis.—As we have said, the course of the disease is extremely variable. Cases in which irritative symptoms with restlessness or delirium predominate tend to last longer and to end fatally more often than those of the common type with lethargy and cranial nerve palsies. It is not possible, however, to speak of any case as mild, since profoundly disabling sequels are as apt to follow a slight and transitory initial attack as one of greater apparent severity, and although relatively few acute cases end fatally in the initial attack, a restoration to normal health is exceptional.

Sequels.—Symptoms indicating focal lesions in the brain may develop at any period after recovery from the initial illness up to three or four years, and certain clinical pictures have come to be recognised as indicating the previous occurrence of such an illness. Of these, the commonest is that of Parkinsonian rigidity. In rare instances such a condition may develop during the acute stage of the malady, but commonly it develops insidiously some months or even years after recovery from this. The patient becomes progressively slower in all his movements, his face takes on the immobility of paralysis agitans, and his gait and stance slowly come to resemble those seen in this disease. This so-called post-encephalitic Parkinsonism in its early stages is most easily seen as the patient moves about and carries on his normal activities, and if it escapes the observer's eye in these circumstances is apt to be missed during a routine clinical examination. The facies is fixed and has a somewhat staring expression, due to slight retraction of the lids. The gait is slow, the arms are not swung normally, and the whole body seems to be held in such a way as to cut down movement to a minimum. When the eyelids are closed they develop a fine tremor, and a similar tremor of the lips and tongue is common. Passive manipulation of the arms reveals a peculiar rigidity of variable degree. The hands have the characteristic posture seen in paralysis agitans, and the tremor of this disease may be present in them. The skin of the face is often greasy, and saliva trickles from the angles of the mouth in the severer cases. In a few instances so-called oculogyric crises occur. The head is drawn back and the eyes turn up, the muscular spasm lasting for as long as half an hour.

Other residual symptoms are persistent weakness of cranial nerves, third, sixth, or seventh, rhythmic muscular twitchings of face or other muscles, bizarre and complicated involuntary movements of the eyes, face, tongue, trunk, or limb musculature, and disorders of respiratory movements.

In children particularly, mental changes may predominate. The child becomes refractory and intractable, and shows disorders of moral conduct. In adults, mental apathy, persistent drowsiness, undue fatigue, and sometimes insomnia are common.

Once these residual symptom-complexes develop they tend to progress, and recovery or material improvement is exceptional.

Treatment.—No drug is known to have any certain influence upon the acute stage of the disease. Favourable results are said to have followed the intravenous injection of sodium salicylate (2·5 per cent. solution in normal saline), 10 c.c. daily for eight days.

As in all infections and intoxications of the nervous system, complete rest in bed is indicated, and should be maintained for at least three weeks after symptoms have disappeared. Return to normal physical activity should be delayed for at least three months.

The treatment of post-encephalitic Parkinsonism is purely symptomatic, and consists in the administration of hyoscine hydrobromide ($\frac{1}{150}$ to $\frac{1}{100}$ gr. by mouth t.i.d.) or of tincture of belladonna or of stramonium in increasing doses (up to 30 minims t.i.d.). It is said that the addition of pilocarpine nitrate ($\frac{1}{15}$ gr.) to each dose increases tolerance.

For the oculogyric crises a hypodermic injection of hyoscine hydrobromide ($\frac{1}{100}$ gr.) may be necessary in the more distressing cases.

For the children who show conduct disorders, institutional treatment may be necessary.

Post-infective Encephalitis

Rarely, a form of encephalitis may appear in association with the exanthemata, measles, smallpox, chickenpox, mumps, and vaccination. It develops suddenly on or about the tenth to the fourteenth day of the illness. There is a cerebral and a spinal (myelitic) form.

The pathological lesion is strikingly uniform and consists of destruction of the myelin sheaths within brain and cord, the nerve cells being little affected. It is probable, therefore, that we are dealing not with a true virus disease of the nervous system but with an intoxication of the nervous system associated with a systemic virus infection.

Symptomatology.—In the *cerebral form* there is a recrudescence of fever; the child becomes somnolent, or delirious, and may have convulsions. Clinical signs of meningitis may be prominent. Cranial nerve palsies, hemiplegia, paraplegia or involuntary movements may all occur, with incontinence of urine and fæces. Papillœdema is common. In most cases improvement begins in three or four days, and the child passes through a phase of irritability to complete recovery. Residual paralysis may be left. Some cases, however, end fatally. The *spinal form* consists of paraplegia of sudden onset with retention of urine and some sensory loss. If death does not ensue within a few days, complete recovery may be expected.

In both forms the cerebrospinal fluid contains an excess of lymphocytes, but the chemical changes of acute meningitis are absent.

HERPES ZOSTER

(*Shingles*)

Clinically, this malady consists in the appearance of an acute vesicular eruption within the distribution of a dorsal spinal nerve root. The pathological process is an acute infective inflammation of a spinal root ganglion, the lesion resembling that seen in the anterior horns of the spinal cord in acute

poliomyelitis, though there is no reason to suppose that the virus in the two maladies is the same.

Ætiology.—On the whole, perhaps, males are more frequently affected than females. It may occur at any age from childhood upwards, though herpes of the ophthalmic division of the fifth nerve is more common in the second half of life. It has a close relationship with chickenpox, and not rarely the latter appears in a household in which some two weeks earlier a case of herpes has developed. Herpes and a generalised chickenpox eruption may occur in the same person.

In most instances herpes zoster develops without any discoverable cause, and we may regard it as an acute infection, probably by a virus, of the sensory root ganglia.

Pathology.—The lesion consists in (i) necrosis of one or more adjacent ganglia with intense lymphocytic infiltration and hæmorrhage ; (ii) a localised poliomyelitis confined to the same side of the cord and to the same segments as the affected ganglia, and more marked in the dorsal than in the ventral horn ; (iii) a mild localised leptomeningitis of the involved segments and nerve roots ; and (iv) a true neuritis of the dorsal and ventral roots and of the nerve roots immediately distal to the ganglion.

The eruption corresponds to the cutaneous distribution of the root of the ganglion most severely affected, and the nerve root lesion probably underlies the neuralgic pains and the motor paralyses sometimes encountered in cases of herpes zoster.

Symptomatology.—As in acute poliomyelitis, there may be an initial febrile reaction of three or four days' duration. The temperature may reach 102° F. in children. There is pain from the outset at the site in which the rash is later to appear, and if the mid-thoracic region be affected, pleurisy may be suspected. The rash appears on the third or fourth day, at one or more of the situations in which the cutaneous branches of the affected nerve root come to the surface, and spreads along the distribution of the nerve twig from this point. The rash develops for from two to six days, appearing first as an erythema upon which vesicles filled with clear fluid subsequently develop. From the fifth to the tenth day the vesicles begin to dry up and scab ; ultimately scarring may be left, particularly if the blisters have broken and any infection of the resulting shallow ulcers has occurred. The pain lasts until the rash begins to heal, and may vary from an uncomfortable itching to intense burning pain. In elderly patients, however, it may persist for months with great severity and prove intractable to treatment. Peculiar to elderly patients is herpes zoster in the distribution of the trigeminal nerve, more especially in that of the first or ophthalmic division. Vesicles appear on the side of the nose and over the brow, and sometimes on the cornea. If the corneal ulcers, which result from bursting of the vesicles, become infected, severe corneal ulceration may ensue. Occasionally there is an associated iritis. Rarely ocular palsies and ptosis may be associated with trigeminal herpes, just as facial palsy may occur with geniculate ganglion herpes (see also Facial Paralysis, p. 665). Sometimes, also, we see paralysis of muscles innervated from the spinal cord segment, the dorsal root ganglion of which is affected. Thus herpes of the seventh and eighth thoracic ganglia may be accompanied by paralysis of the rectus and oblique muscles of the abdominal wall. All these paralyses tend to recovery.

Herpes labialis and herpes febrilis are not related to herpes zoster.

Treatment.—The course of the eruption is uninfluenced by treatment. The vesicles are best dusted with a starch or zinc oxide powder, or a collodion dressing may be applied over the whole affected skin area. The latter measure is the better when the situation of the eruption allows of it, since it protects the burst vesicles from secondary infection and from friction and appears to have some analgesic value. Post-herpetic neuralgia is difficult to relieve, and on occasion it may be necessary to use morphia in aged and debilitated subjects whose sleep is impaired by pain. Before recourse is had to this, however, aspirin, phenacetin and caffeine citrate, or luminal or tincture of gelsemium and bromide may be tried.

SYPHILIS OF THE NERVOUS SYSTEM

Hitherto syphilis has been regarded as the most important single factor in the causation of organic nervous disease, but with the diminishing incidence of primary syphilis it is probable that neurosyphilis will no longer maintain its sinister position in this respect, if, indeed, disseminated sclerosis is not already as common a malady as neurosyphilis in all its forms.

There is still much that is uncertain in the pathology of syphilis as it affects the nervous system, but the following brief summary represents the most widely accepted body of opinion in respect of two important points in the ætiology of neurosyphilis.

1. The Mode and Period of Invasion of the Nervous System.—In a small proportion of cases of primary syphilis, at a stage when the Wassermann reaction in the blood is still negative, examination of the cerebrospinal fluid reveals signs of a meningeal reaction, namely, an increased lymphocyte and globulin content in the fluid. This proportion steadily increases through the primary stage of syphilis, and during the acute secondary stage approximately 50 per cent. of all syphilitics present signs of a brisk meningeal reaction.

This reaction is undoubtedly due to invasion of the meninges by the spirochæte, and it is now believed that such a meningeal inflammatory reaction is an essential condition of invasion of the central nervous system by spirochætes, and that when such invasion occurs it is at this early stage of infection and at no other. It appears, therefore, that the foundations of subsequent neurosyphilis are laid during the primary and acute secondary stages of the infection. Unfortunately, in the present state of knowledge we cannot tell whether, in a given case, the meningeal reaction is accompanied by invasion of the nervous tissues, since this invasion in the great majority of cases gives rise to no special symptoms at this stage.

Usually, whether invasion has occurred or not, the cerebrospinal fluid returns to a normal state. If invasion has not occurred it remains normal, but in other cases it later presents evidence of a fresh meningeal reaction, which responds incompletely, if at all, to anti-syphilitic treatment. It is in such cases that the later development of neurosyphilis is to be feared.

It is probable that the meninges are the sole channel of access of the spirochæte to the nervous system.

2. The Lesion of Neurosyphilis.—The invasion of the central nervous system gives rise to no signs of pathological change for a period of years in most instances, and the cause of this latency has not yet been satisfactorily explained. It cannot be due to an extremely slow process of parenchymatous

degeneration of nerve cells and fibres, and is more likely to be due to a delayed hypersensitiveness of a parenchyma actually invaded long since. Histological investigations of the lesions in neurosyphilis indicate that there are two main types of lesion : a so-called meningo-vascular syphilis, in which there are signs of active pathological change in vascular and supporting tissues, with inconsiderable damage to the nervous elements ; and a so-called central or parenchymatous syphilis, in which signs of meningo-vascular lesions are inconsiderable and not active, and in which degenerative changes in nerve cells and fibres predominate.

It was formerly supposed that these lesions represented two essentially distinct syphilitic processes, but it is now widely accepted that parenchymatous lesions are invariably secondary to meningo-vascular changes, although these may have ceased to be active long before the clinical signs of parenchymatous degeneration appear. Further, the view that the lesions of so-called parenchymatous syphilis are systemic, involving certain neuronal systems and these alone, has also been found to be untenable, thus removing one of the strongest grounds for a belief in a pure neuronal degeneration as a special expression of neurosyphilis.

We may say, therefore, that in the nervous system, as elsewhere in the body, the essential lesion of syphilis is an arteritis, with which is associated a perivascular lymphangitis, and a meningitis when the vessels affected lie in the meninges. The arteries show intimal thickening with perivascular infiltration of the adventitia by lymphocytes and plasma cells. Such a lesion forms the basis of gumma formation. The details of the lesion in the several varieties of neurosyphilis will be considered when these are described.

The Cerebrospinal Fluid in Neurosyphilis.—Some further details on this subject are necessary.

1. *Primary and Secondary Stages.*—During the primary stage of syphilis, a meningeal reaction is present in from 15 to 20 per cent. of cases. The earliest change is an increase in the lymphocyte content of the fluid. As the secondary stage advances, the lymphocytes increase in number, ranging from 25 to 100 or more per cubic millimetre ; also some polymorphonuclear and plasma cells may be seen. Protein excess does not usually appear until the secondary stage is reached. A positive Wassermann reaction is exceptional, occurring in some 10 to 15 per cent. of cases.

After the passing of the acute secondary stage, whether the case be treated or not, the lymphocytosis disappears or becomes considerably reduced, but a recurrent and very brisk meningeal reaction may develop, occasionally associated with clinical signs of neurosyphilis (optic neuritis, cranial, and spinal nerve lesions). A high pleocytosis may now be found in the cerebrospinal fluid, amounting to 1,000 cells per cubic millimetre (lymphocytes, polynuclear, and plasma cells), together with a strongly positive protein and Wassermann reaction. This reaction is generally responsive to active antisyphilitic treatment.

2. *Latent Period.*—The second and third years after infection. During this period about a fifth of all cases of syphilis present a lymphocytosis, protein excess, and positive Wassermann reaction in the fluid. If the fluid be normal during this period the subject is unlikely to develop neurosyphilis later, but there is no high degree of certainty on this point, as normal cerebrospinal fluids have been found at this stage in syphilitic subjects who later develop general paralysis. This is probably an exceptional state of affairs.

3. *Tertiary Syphilis.*—Unless there is syphilitic meningitis the fluid at this period will be normal. In acute syphilitic meningitis at this stage the cerebrospinal fluid contains up to 500 lymphocytes per cubic millimetre, up to 100 mg. of protein per 100 c.c., and a strongly positive Wassermann reaction. The blood Wassermann is also positive. In chronic syphilitic meningitis these changes are present, but are of less intensity than in the acute process.

In syphilitic cerebral vascular disease there will be no characteristic changes in the cerebrospinal fluid unless there be an associated meningitis. A relatively low lymphocytosis and protein increase, with or without a positive Wassermann reaction, is the rule. The blood Wassermann is positive. In cases of syphilitic hemiplegia a negative cerebrospinal fluid Wassermann may be obtained in about half the cases.

In congenital syphilis the cerebrospinal fluid shows very inconstant changes, but with juvenile tabes or general paralysis the characteristic changes in the fluid are found.

4. *In Tabes Dorsalis* cerebrospinal fluid changes of moderate intensity are the rule. The cell count varies from 10 to 80 lymphocytes per cubic millimetre. There is a slight or moderate increase in protein and a positive Wassermann reaction in blood or fluid, or in both. The last-named reaction is negative, however, in the fluid and blood in 25 per cent. of cases. When a positive fluid Wassermann is present it is rarely influenced by anti-syphilitic treatment. A reduction in the cell count is more easily obtained, but is not necessarily accompanied by any improvement in the clinical condition. Further, the clinical progress of a case of tabes dorsalis is not necessarily reflected by the condition of the cerebrospinal fluid, which is, in consequence, of little value as a guide to treatment.

5. *In General Paralysis of the Insane* the pressure of the cerebrospinal fluid is raised, the cell count may range from 50 to 200 cells per cubic millimetre (lymphocytes, mononuclears, plasma cells, macrophages). The protein content is increased, and the Wassermann reaction is always positive in the fluid and almost always so in the blood. Apart from the cell count, which always falls as a result of repeated lumbar puncture alone, these abnormalities are irresponsive to treatment.

Colloidal Reactions in the Cerebrospinal Fluid.—In certain nervous diseases the protein content of the cerebrospinal fluid undergoes an increase, the albumin fraction always exceeding in amount the globulin fraction of this protein. In neurosyphilis and in disseminated sclerosis, however, the globulin is relatively high and almost equals the albumin present. Associated with this relatively high globulin content, the cerebrospinal fluid develops the power of precipitating the particles of a colloidal suspension to which it is added. It has been found that colloidal gold is delicately responsive in this way, a fact that is the basis of Lange's colloidal gold reaction which is carried out as follows: a constant quantity of a standard suspension of colloidal gold is added to 10 graded dilutions of cerebrospinal fluid (from 1 in 10 to 1 in 10,000). In general paralysis the gold is precipitated in the first six dilutions; in tabes, precipitation is maximal in the third and fourth dilutions; while in meningitic fluids precipitation is greatest in the sixth to eighth dilutions. Thus so-called paretic, luetic, and meningitic curves can be plotted.

In disseminated sclerosis the combination of a negative Wassermann reaction in the fluid with a paretic curve is found.

The practical importance of these reactions can easily be overestimated.

The occasions on which they provide information not otherwise obtainable are limited. Thus it is rare indeed that a diagnosis of disseminated sclerosis really depends upon the result of this reaction, and its chief value is in differentiating certain cases of general paralysis from those of meningo-vascular cerebral syphilis. In the former anti-syphilitic treatment leaves the reaction unchanged, but in the latter a change from a paretic to a luetic curve may occur.

CEREBROSPINAL SYPHILIS

The form of syphilis in which the lesions are predominantly meningo-vascular may involve the brain and cord separately, or both together. The morbid anatomy is the same in each case, but the clinical pictures will be described separately.

The onset of symptoms is generally first noted towards the end of the five-year period after infection, but there are sometimes clinical indications of acute syphilitic meningitis during the secondary stage of syphilis.

Morbid Anatomy.—It has been stated that the essential syphilitic lesion in the nervous system, as elsewhere in the body, is an arteritis. In the nervous system there is an associated perivascular lymphangitis. It is the vascular and supporting tissues which are thus primarily involved, the nervous elements being secondarily affected by pressure, infiltration, or intoxication. The multiplication of the spirochæte in the perivascular lymph spaces leads to an inflammatory reaction with cellular infiltration. This may take the form of a diffuse vascular granulation tissue, or of local gummatous masses. *Gummata* generally arise either in the dura or in the pia-arachnoid, the latter being the more common situation. They form nodules of varying shape, and when they occur over the convexity of the hemisphere they are lentiform, compressing and infiltrating the subjacent brain, and sometimes giving rise to the signs of cerebral tumour. At the base of the brain they tend to form small nodules situated in a mass of thickened and inflamed pia-arachnoid and forming part of a gummatous meningitis. *Gummatous meningitis* may occur over any part of the brain, but is most frequent in the interpeduncular space, where it involves the meningeal sheaths of the cranial nerves and of the chiasma. To the naked eye the pia-arachnoid is thickened and gelatinous, and the subarachnoid space contains exudate. The vessels entering into and derived from the circle of Willis are also involved.

Syphilitic meningo-myelitis is the common form of spinal syphilis and is a pathological process like that already described. The lesion is generally localised to several adjacent segments of the cord, and tends to produce the signs of a focal transverse cord lesion. The pia-arachnoid becomes adherent to the subjacent cord, which is infiltrated by the gummatous process with the production of a varying degree of myelitis.

Involvement of the spinal dura leads to the production of *pachymeningitis cervicalis hypertrophica*, a condition of primary thickening of the dura which in the cervical region is swollen, hard, and may completely fill the vertebral canal. The nerve roots are compressed and atrophy, and the cord itself undergoes some degree of constriction, and shows a varying degree of secondary sclerosis sometimes with cavitaton.

Symptomatology—(*a*) **Cerebral Syphilis.**—There are two clinical types of cerebral syphilis : that produced by gummatous meningitis at the base of the

brain, and that due to syphilitic endarteritis of the central branches of the middle cerebral artery. In both forms the development of objective physical signs is preceded by premonitory symptoms. These are headache, sometimes of great severity and usually worse during the night, and mental and emotional changes of varying degree. The fine edge is taken off the patient's intellectual capacity and he becomes forgetful and irritable. Delirium or apathy may be present. After some weeks or months of this prodromal stage, objective signs develop. In the case of gummatous meningitis the signs are cranial nerve paralyses, which may be unilateral, although the pathological process is bilateral. Pupillary abnormalities (myosis, inequality, and irregularity of outline, deficient or absent light reaction), squint, diplopia, ptosis, deafness and tinnitus, facial weakness and sensory changes over the face, all serve to indicate the nerves involved. With meningitis on the convexity of the hemispheres, Jacksonian fits and transient hemiparesis or aphasia may be present.

In syphilitic endarteritis obliterans of the central branches of the middle cerebral artery, cerebral thrombosis may result with hemiplegia. The symptomatology of this condition has already been described in the chapter on Cerebral Vascular Disease (*vide* p. 597).

(*b*) **Spinal Syphilis.**—Although the clinical pictures of spinal syphilis vary greatly and fall into several groups, the underlying pathological process is remarkably uniform, varying more in acuteness than in kind.

1. Transverse Meningo-myelitis.—This may be a process localised to a few segments of the cord and productive of the symptoms of a transverse lesion of the cord, a transverse myelitis. Like the signs of cerebral syphilis, those of spinal syphilis are preceded by premonitory symptoms. These are pain in the back, girdle, or other root pains, and numbness in the extremities. Signs of interference with the functions of the cord come on with a rapidity which varies from case to case. Where there is much arterial disease with softening of the cord, paraplegia with sensory loss and sphincter paralysis develop with great rapidity, and an almost complete transverse lesion may ensue within a few days. The abdominal reflexes are lost below the level of the lesion, which is commonly mid-thoracic ; there is sensory loss and weakness of the legs that may be spastic from the onset or rapidly become so, often with retention or distension with overflow. In severe cases, total paraplegia with bed-sores may be present.

2. Erb's Syphilitic Paraplegia.—A much less acute and more slowly progressive form of meningo-myelitis of the thoracic region of the cord is known by this name. There is relatively little weakness, but when the patient is standing or walking the legs become intensely spastic and the gait is spastic and shuffling. There is also little cutaneous sensory loss, but more marked loss of the sense of position and of vibration sensation. The sphincters, also, are severely impaired. The condition may be present for many years before the power of walking is lost. Root pains may be a prominent symptom.

3. Amyotrophic Meningo-myelitis (spinal progressive muscular atrophy of syphilitic origin).—A form of meningo-myelitis affecting the cervical region of the cord may produce a clinical picture closely resembling that of progressive muscular atrophy. The signs are atonic atrophy beginning in the small hand muscles, in the shoulder muscles, or in those of the leg. This may be unilateral or bilateral, and is often preceded by root pains. There may be spastic paresis of the legs, some impairment of vibration sense in the legs, and loss of sphincter

control. The Argyll-Robertson pupil is present in an appreciable proportion of these cases. The blood Wassermann reaction is positive in two-thirds of the cases, and the cerebrospinal fluid gives a positive reaction in all untreated cases. This condition may be present in association with tabes dorsalis.

4. Pachymeningitis Cervicalis Hypertrophica.—In this there are root compression symptoms : pains radiating down the arms, wasting and weakness of arm and hand muscles, with alterations in the arm jerks and sensory impairment. The legs show a condition of spastic weakness.

Diagnosis.—These various clinical forms of spinal syphilis may have to be differentiated from several spinal cord diseases : infective myelitis, disseminated sclerosis, compression of the cord, progressive muscular atrophy. In all cases the examination of the blood and cerebrospinal fluid should be made, and other signs of syphilis sought for. Pupillary abnormalities of the type described above may afford the necessary clinical confirmation. A history of syphilitic infection is of importance, though the absence of such a history is of no value.

These criteria must also govern the differential diagnosis of cerebral syphilis. It must be remembered that both cerebral tumour and syphilitic infection are common occurrences, and that the presence of a positive blood Wassermann reaction in a case of suspected cerebral tumour is not adequate reason for regarding the latter as a gumma.

Prognosis.—Recent cases of cerebral syphilis or of spinal meningo-myelitis respond well to energetic anti-syphilitic treatment. Long-standing cases, on the other hand, respond less well, and even though the pathological process be arrested, some residual disability tends to remain. Erb's syphilitic paraplegia usually responds little if at all to treatment, while amyotrophic meningo-myelitis may be arrested but seldom cured in the sense of recovery.

DEMENTIA PARALYTICA

(*General Paralysis of the Insane*)

This is essentially a syphilitic affection. Males are affected far more frequently than females. The onset occurs from ten to twenty years after primary infection, that is, commonly between the ages of thirty to forty-five. The percentage of syphilitic subjects who develop this malady is probably extremely small. Occasionally the subjects of congenital syphilis develop the disease in childhood.

Morbid Anatomy.—The skull bones are dense, and beneath the dura there may be signs of old subdural hæmatomata (chronic hæmorrhagic pachymeningitis). The brain is shrunken and diminished in weight. The pia-arachnoid is thickened and opaque, and may be adherent to the subjacent brain. The convolutions are atrophic and the sulci correspondingly wide. The ependyma is " frosted " in appearance and is seen to be studded with tiny, closely set granules. Microscopically, the maximal degree of change is found in the frontal lobes ; the vessels are dilated and show signs of proliferation ; their walls are thickened, and the perivascular spaces infiltrated with lymphocytes, plasma, and other cells. There is marked neuroglial reaction. The nerve cells reveal various stages of chromatolytic degeneration, and the superficial nerve fibres are also degenerated. Spirochætes may be found.

Symptomatology.—There are various clinical pictures characteristic of the disease, especially in its earliest stages. In some subjects mental deterioration is the earliest symptom. In others objective neurological signs are prominent from the first, with corresponding symptoms.

Mental Symptoms.—The essential feature is a slowly progressive deterioration of the intellect, the most complex and most recently acquired faculties being first and most severely hit. Judgment, memory, and receptivity begin to fail. The standard of conduct falls off, and the patient becomes careless of the conventions and may develop moral aberrations. He becomes suspicious and irritable, and impatient of any kind of restraint. He may be sullen and depressed, or exalted and boastful. He uses his financial resources rashly and may ruin his family as a result. The familiar picture of grandiose ideas with absurd boastfulness is, perhaps, not the common one, and most patients are depressed and introspective. These changes develop gradually and are best noticed by the patient's immediate family circle, which suffers most severely from his aberrations. With the passing of time, memory and judgment progressively fail, and ultimately a severe grade of dementia develops.

Associated with this mental picture is the presence of objective physical signs of organic nervous disease. In the early stages these are: unequal and irregular pupils which react badly to light, tremor of the lips and tongue and of the hands. Articulation is slurring. Defects in the speech function appear later. A partial primary optic atrophy is common. The reflexes show progressive alteration, the tendon jerks becoming brisker than normal and the plantar responses becoming of the extensor, or Babinski, type. Gradually bilateral spastic paresis develops, with loss of sphincter control, and ultimately the patient becomes a helpless bedridden dement. This progress is punctuated in the early stages by transient apoplectiform and epileptiform seizures, the so-called congestive attacks. They are associated with transient hemiplegia or aphasia. Again, acute maniacal outbursts or sudden phases of exaltation may occur. Remission of symptoms is common, the patient improving in a most remarkable fashion and retaining the improved level of mental and physical health for some months.

Occasionally the symptoms of general paralysis may be associated with certain signs of tabes dorsalis, the so-called taboparesis. The clinical course of this condition, however, is much slower and longer drawn out than that of general paralysis alone.

Course and Prognosis.—The malady usually runs its course to a fatal issue within three or four years. More acute cases occur in which death ensues within a year. The various clinical varieties have each their characteristic course and duration.

Diagnosis.—This may present difficulties in the initial stages in those cases in which objective signs are scanty. The patient has no insight into the alteration in his mental and emotional state, which may not be evident unless an independent history can be obtained from his relatives. In many cases it is by information derived from a patient's wife that the presence of definite mental deterioration can alone be discovered, and the patient's story should always be compared with that obtained from some competent witness. It is in the case of the depressed hypochondriac subject that these difficulties are most in evidence, and a diagnosis of neurasthenia should be made with reserve in a middle-aged man of this type until general paralysis has been definitely excluded by careful clinical examination and examination of the

blood and cerebrospinal fluid. The objective signs to be sought for are pupillary abnormalities, tremor of the lips and tongue, slight slurring of speech, and alterations in the reflexes.

Another source of difficulty is the close resemblance which some cases of cerebral syphilis bear to general paralysis, and in this case a differential diagnosis may be impossible without some period of observation and one or more examinations of the cerebrospinal fluid (*vide* p. 635).

Treatment will be dealt with later (*vide* p. 646).

TABES DORSALIS

This common malady of the nervous system is essentially syphilitic in origin. It makes its appearance from five to twenty years after infection, and is much more common in men than in women. It is occasionally a result of congenital syphilis, and like general paralysis may exist in husband and wife when one partner has acquired syphilis from the other.

Morbid Anatomy.—On naked-eye inspection the dorsal columns of the cord are seen to be shrunken and translucent in appearance on section of the cord. The dorsal roots are also similarly shrunken and have a pinkish, gelatinous appearance. The change is most marked in the lumbar and thoracic regions of the cord. Other evidence of neurosyphilis may be present, such as basal meningitis and meningo-myelitis.

The evolution of the essential lesion in tabes is still a matter of controversy. While the signs and symptoms of the disease are a consequence of the degeneration of the exogenous fibres of the posterior columns of the cord, as these lie in the root entry zone, it is probable that this degeneration is not a primary parenchymatous change but is secondary to a local meningitis of the posterior roots outside the cord.

The short and medium length fibres tend to degenerate earlier than the long fibres and, like other nerve fibre degenerations, this process does not extend beyond the synapse in which the affected fibre ends. The degeneration in tabes is therefore confined to the exogenous dorsal root fibres, and can be traced up through the dorsal columns of the cord from lumbar region to the posterior column nuclei in the medulla. The cranial nerve palsies which are sometimes seen in cases of tabes are due to a meningo-vascular process such as has already been described. The primary optic atrophy of tabes is also the result of a similar process in the sheath of the optic nerve, and is not, as was formerly supposed, a primary syphilitic degeneration of the optic nerve neurones.

The pupillary changes of tabes are even more obscure in their origin than is the essential lesion of this disease. Neither the view that there is a degeneration of light reflex fibres nor that which invokes changes in the ciliary nerves is entirely satisfactory, and the question remains an open one.

A common post-mortem finding in subjects dead of tabes is a syphilitic aortitis or aneurysm.

Symptomatology.—Since tabes dorsalis develops very slowly, not all its physical signs are equally early in development, and the malady may be readily recognisable at a time when some of its so-called cardinal signs are absent. Further, it may be arrested at any stage of its evolution and thus continue indefinitely to present an incomplete clinical picture. Hence the old

division of the clinical course into "pre-ataxic" and "ataxic" stages is fallacious and useless. Finally, in some cases there is no noticeable disability or subjective symptom which is obviously nervous in origin, and the disease may be discovered only during the course of a routine examination of the patient. Since it is a disease of the primary afferent neurone its signs and symptoms must necessarily be of the following character: pains and paræsthesiæ, sensory impairment, ataxy of movement of sensory origin, loss of tendon reflexes, muscular hypotonia. To these we may add impairment of sphincter control and of sexual desire and power, trophic lesions, and pupillary anomalies.

In its early stages the common subjective symptoms are pains. The most typical of these are the "lightning pains" which are very rarely absent and which may antedate all other symptoms by a period of years. Since the tabetic lesion is in the lumbar and thoracic regions of the cord, these pains are present in the lower limbs and trunk. They are sharp and sudden in incidence, and come in paroxysms which are more severe and frequent in wet, cold weather. They rarely run up or down the length of the limb, but seem to strike into the limb from outside and are described as "stabs of pain," "like a needle being stuck into the leg." They are common in the heel, calf, and region of the foot. Pains of a similar character may be present in the thoracic wall.

These pains vary in severity, and when not intense may be interpreted by the patient as due to "rheumatism" or some other supposedly minor ailment, and may thus not be seriously regarded by him. Various other pains and paræsthesiæ in limbs and trunk may also be complained of.

On examination the following objective sensory disturbances are usually found. Over the front of the thorax, from the level of the second rib to that of the lower costal margin, where it forms a cuirass of sensory change, is an area of analgesia, and sometimes of tactile and thermal anæsthesia or hypoæsthesia also. This area may extend down the medial aspect of the upper limbs to the little and ring fingers. The region of the perineum may also be similarly insensitive, especially in those patients in whom alteration in sphincter control is an early symptom. In respect of deep structures, the tendo Achillis is almost always painless on pressure, or if painful sensibility be retained in any degree, its conduction is delayed and the patient cries out one or more seconds after pressure is put upon the tendon. The ulnar nerve at the elbow may also be relatively insensitive to pressure. Over the nose and upper lip, in those patients with an Argyll-Robertson pupillary reaction, there is commonly an area of analgesia, the so-called tabetic mask of Duchenne. Examination of the limbs for the sense of position may reveal some impairment. Passive movement of the great toe, the patient having his eyes shut, may be possible through an abnormally wide range before it is perceived, and in the heel-knee test, carried out under the same conditions, the error of projection of the heel may be considerable. When this form of sensory loss is marked there will be some degree of ataxy of gait, or if not, then some Rombergism will be present. That is to say, when the patient is deprived of the use of vision the impairment of sense of position leads to some unsteadiness of stance and to swaying that does not occur when vision is employed. Rombergism is a sign of defect in the sense of position in the legs and will occur in any malady in which there is this form of sensory disturbance. It must be emphasised, however, that in the early stage of progressive tabes, or

in arrested cases, neither Rombergism nor ataxy of stance or gait may be present. In cervical tabes, similar disorders of the upper limbs may be found.

The Reflexes.—The afferent limb of the reflex arcs concerned in these reactions being involved, the tendon jerks in the legs slowly diminish in activity and finally disappear. The first to go are the ankle jerks, and their disappearance may precede that of the knee jerks by a considerable period. Therefore retention of the knee jerks does not necessarily exclude the presence of recognisable tabes. The arm jerks tend to go even later than the knee jerks and may be retained for an indefinite time, excepr in involvement of the cervical posterior root fibres.

The Pupils.—From the onset of the disease the pupils become progressively smaller, and ultimately a high degree of myosis obtains. Simultaneously they lose their circular outline and become unequal in diameter and the reaction to light wanes until it is lost. While this loss of reaction to light is perhaps the most important feature of the pupillary changes in tabes, myosis is, sooner or later, an almost invariable accompaniment of this loss and was so regarded by Argyll-Robertson after whom the phenomenon is named. Reaction to accommodation is retained until the terminal stage of the malady, when it too may be lost.

The common sphincter defect is hesitancy of micturition with a tendency to dribbling incontinence after a voluntary act of micturition. Impairment and early loss of both sexual desire and power is a very common symptom at this stage of the malady but is not invariable. The cutaneous reflexes (abdominal and cremasteric) are retained and are usually very brisk throughout the malady. The plantar responses are of normal type.

We may sum up the signs and symptoms of early tabes dorsalis, or of non-progressive cases of the disease, as follows: lightning pains, objective sensory disturbances on face, trunk, and lower limbs, diminution or loss of the knee and ankle jerks, the presence of Rombergism or of ataxy of gait and stance in a proportion of patients, but not in all, the presence of a varying degree of abnormality in the appearance and reaction of the pupils, and some defect in sexual function and in sphincter control.

In the more advanced stage of progressive cases, the physical signs mentioned above become more evident, though the characteristic pains may wane and almost cease except as occasional phenomena. The loss of sense of position in the legs leads to marked ataxy, sometimes of a degree which completely takes the patient off his feet and gives him a superficial appearance of being partially paralysed. However, bed tests of muscular power reveal that this is not impaired, although co-ordination may be grossly disordered. The arms may be similarly affected.

Sensory loss tends to involve larger areas of the trunk and limbs, although the abdominal wall retains sensibility in some patients for a long period.

All the tendon reflexes may disappear. In the terminal stages of tabes the pupils become extremely small and the reaction to accommodation is commonly lost, the pupils being immobile.

Sphincter control tends to become more defective, and incontinence of urine may be a distressing symptom. It is often accompanied by profound loss of sensation over the perineum and in the external genitals, so that the passage of urine and fæces, and even of a catheter, cannot be felt. The bladder invariably contains several ounces of residual urine and is commonly infected.

The presence of chronic infection from this source is in part responsible for the pallor and cachectic appearance of most tabetics of long standing.

Among the inconstant symptoms of tabes are the following :—

Ataxy.—Many cases of tabes run their whole or a great part of their course without the development of this disability. Its absence indicates the integrity of those afferent fibres which subserve the sense of position and of movement. On the other hand, gross ataxy of the lower limbs may develop acutely, either spontaneously or after confinement of the patient to bed from injury or some intercurrent malady. Such an acute ataxy may first draw attention to the malady in cases which have previously been free from marked subjective symptoms of any kind. When it is severe in degree, standing may be quite impossible owing to the complete absence of control of movement. In less severe grades the patient stands with a wide base, and as he walks keeps his gaze intent upon his feet. These are raised overhigh and are stamped down, heel first, with undue force. The legs are widely separated and perform many adventitious movements from the combined effects of ataxy and voluntary efforts at correction.

Visceral Crises.—Of these the commonest is the gastric crisis, which in its complete form consists of an attack of acute abdominal pain with vomiting, lasting for from two or three to seven or more days. The vomiting may be severe and provoked by food. Hypersensitiveness of the skin over the epigastrium is a common accompaniment of gastric crises and may be present in the subject at other times. In some instances vomiting may occur without pain. Tabetic patients with gastric crises are frequently subjected to laparotomy on an erroneous diagnosis of some acute local lesion when a routine examination of the nervous system has not been made, an occurrence which is rendered the more easy as the patient may, spontaneously, make no other complaint than one of pain and vomiting.

Less frequent are laryngeal crises, attacks of stridor and dyspnœa occurring at short intervals over a period of one or more hours. Abductor paralysis of the vocal cords may follow a laryngeal crisis as a temporary state or may be a permanent condition apart from crises. Attacks of tenesmus (rectal crises) or of painful micturition (vesical crises) are also known.

Although the subject may be very distressed during the period of a crisis, a fatal termination does not occur.

Optic Atrophy.—In an appreciable number of tabetics, optic atrophy develops and leads to progressive failure of vision, and generally to blindness, with the ophthalmoscopic appearance of a primary atrophy of the disc. The two eyes are generally affected, but not simultaneously. It was formerly held that the presence of optic atrophy led to an arrest of the tabetic process in the so-called pre-ataxic stage, but a more correct way of expressing the rarity of advanced tabes in the subjects of optic atrophy is to say that in those cases in which the two lesions coexist the optic nerve bears the brunt of the disease. Tabetic optic atrophy is invariably accompanied by the Argyll-Robertson pupil and generally by loss of both knee and ankle jerks, and by the cutaneous sensory changes described above.

Trophic Lesions.—These may involve the skin and subcutaneous tissues, or joints and bones. The perforating ulcer on the ball of the foot is the familiar example of the former. It usually arises under a pre-existent callosity. This becomes separated from the deeper tissues, a blister or

hæmorrhage occurs, the deep tissues become infected, and the callosity sloughs out, leaving a septic ulcer which does not heal.

It not infrequently happens that the patients in whom this occurs seek medical advice for this lesion and not on account of any other tabetic symptoms. The malady tends to run a peculiarly latent course in those cases where this superficial lesion occurs, and is often non-progressive. The osteo-arthropathy of Charcot (Charcot's joint) is the other familiar trophic lesion. The change is generally precipitated by some injury or strain on the joint. A rapid, painless effusion into the joint cavity follows, and then bony changes begin. These may consist of rarefaction, or of rarefaction accompanied by irregular new bone formation. Destruction of the joint surfaces follows. The joint soon becomes abnormally mobile, and a condition of flail joint ensues when the knee is involved. Other joints affected are the ankle, hip, wrist, and elbow. In syringomyelia a similar condition is not uncommon, the upper limb joints being the usual seat of the lesion in this case. The lumbar spine is sometimes affected. Rarefaction of long bones may lead to spontaneous fracture. As with perforating ulcers, the case may in other respects run a latent non-progressive course.

Ocular Palsies and Amyotrophy of the upper limb muscles may occur in tabes from associated syphilitic meningitis. Ptosis, squint, and diplopia, especially the first-named, are the common cranial nerve palsies. The ptosis together with the myosis gives the patient a characteristically sleepy appearance.

Visceral syphilis may also be present in the subjects of tabes, syphilitic aortitis and aortic aneurysm being the commonest lesions. General paralysis or spinal meningo-myelitis may also complicate tabes.

Juvenile tabes in congenital syphilitics is comparatively rare, and when it occurs is associated with optic atrophy more frequently than is the tabes of acquired syphilis. The familiar stigmata of congenital syphilis may be absent from the subject of juvenile tabes.

Diagnosis.—Although tabes is a common malady, and one readily detected by even the most rapid routine examination of the nervous system, there are few nervous diseases in which diagnosis is so often unwarrantably delayed or so frequently missed. Among the reasons for this is the fact that observers expect to find the sum total of physical signs at every stage of the malady, and some of these being absent—as they invariably are in the initial period of its development—they either fail to identify the disease or shrink from the responsibility of diagnosis upon incomplete evidence. Another important factor is the extremely variable subjective early symptomatology of tabes. Thus the patient may seek medical advice for attacks of abdominal pain and vomiting, for failure of vision, for diplopia, for pains in the legs, for joint lesions, or for bladder disturbances. Exclusive attention to the local symptom leads to a neglect to examine the nervous system and to a failure to recognise the presence of tabes. Moreover it is a common experience that the subject of lightning pains, having decided that he has rheumatism in his legs, answers the question as to the presence of pain by a negative.

Early diagnosis rests upon the presence of lightning pains, the sensory changes described above, diminished or absent ankle jerks—the knee jerks being possibly normal—pupillary abnormalities, loss of pain sense in the tendo Achillis, and loss of testicular sensation. A history of syphilitic infection and the presence of any one of the above signs should lead to a suspicion of tabes

and to an investigation of the blood and cerebrospinal fluid. The changes in the latter are described elsewhere (*vide* p. 636).

Among the other diseases from which tabes has to be differentiated is multiple peripheral neuritis. In this malady the muscles are usually tender to pressure, there are no pupillary anomalies, no sphincter defects, while there is motor weakness with wasting. The history also affords important points of distinction. The presence of signs of lateral column sclerosis, of a familial history, and the age of the subject should render the differentiation of Friedreich's ataxy simple. Subacute combined degeneration of the spinal cord is also a malady in which the tendon jerks may be lost and the gait ataxic, but no error of diagnosis should arise, for in this disease the leg muscles are commonly tender to pressure, there is muscular weakness, usually an extensor plantar response, and usually, though not necessarily, the signs and symptoms of pernicious anæmia. There is no loss of sphincter control in this disease, except possibly in its terminal stages.

Course and Prognosis.—The course of the malady is extremely variable from case to case. In some, acute ataxy brings it first under notice, while in others the subjective symptomatology and the disability remain trifling for an indefinite number of years until the patient succumbs to some other malady. Arrest may take place at any stage, and this even in cases where both blood and cerebrospinal fluid changes would seem to foretell a rapid progress of the malady. Perhaps approximately 50 per cent. of all cases of tabes undergo arrest at some period short of profound disability. Nor is an early onset of acute ataxy necessarily of bad ultimate prognosis, since with suitable re-education exercises co-ordination may be restored and remain normal for a period of years. It is probable that the shorter the interval between syphilitic infection and the development of tabes, the more progressive and disabling the latter will be. The development of optic atrophy almost always means that the subject will become blind within five years.

This extreme variability of progress and the frequency of arrest should lead to considerable caution in assessing the value of treatment in any given case, and much sanguine opinion in favour of this or that remedy is based upon disregard of the natural variability of the disease.

TREATMENT OF NEUROSYPHILIS

The advent of penicillin appears to have placed a new and potent agent in our hands, and it may now be said that the three agents now available are bismuth, arsenic, and penicillin, and, in addition, when there is reason to think that general paralysis may ensue—or is present—pyrexial therapy.

It will be realised that degeneration of nerve cells and nerve fibres within the central nervous system is irreparable, and that in many long-standing cases of neurosyphilis it is not reasonable to expect more than arrest of active pathological changes in the nervous parenchyma.

In all probability the occurrence of late neurosyphilis with its often disastrous effects is the consequence of the inadequate treatment of syphilis in its initial stages. Therefore the most effective treatment of neurosyphilis is prophylaxis.

In its early stages neurosyphilis is commonly asymptomatic, its presence being discovered only by examination of the cerebrospinal fluid, though

this should not be attempted in any case of early syphilis until a full course of treatment has been completed, a rest period of six months allowed, and the Wassermann reaction in the blood then tested. If it remain positive, then cerebrospinal fluid examination becomes necessary as a guide to further treatment and as an index of the presence or absence of neurosyphilis.

1. *Asymptomatic neurosyphilis* (revealed by the presence of an excess of lymphocytes, of total protein, and of globulin in the fluid, of a change in the colloidal gold reaction, and of a positive Wassermann reaction). A full course of penicillin (preferably crystalline penicillin LL (G)) is given, *i.e.*, 60,000 units three-hourly for ten days, or in a patient who remains at work 300,000 units twice daily for the same period. Also ten intramuscular injections of bismuth (1 to 1·5 c.c. of a suspension of metallic bismuth) at weekly intervals, and ten weekly injections of arsphenamine, intramuscularly, beginning with 0·3 gm., rising to 0·6 gm.

2. *Early acute syphilitic meningitis, meningo-vascular late neurosyphilis, tabes dorsalis, and general paralysis* all receive this course, but in the case of the last named the initial course of penicillin should be followed by pyrexial therapy, and this by a further course of penicillin.

Pyrexia may be achieved either by infecting the patient with benign tertian malaria and allowing him to have up to twelve rigors before exhibiting quinine, or by placing him in an apparatus in which he is electrically heated until a temperature of 104° and upwards is reached, and maintained for the requisite period on a number of occasions. Both these methods are not free from danger and should be undertaken only by those skilled in their use and under ideal conditions. It is not therefore necessary to describe either method in detail here. Seeing that general paralysis when untreated is always a fatal malady the risks involved in these procedures are well justified in early cases where no marked physical disability or profound dementia is present.

It is probable that the treatment acts by the destruction of spirochætes by the pyrexia. Parenchymatous changes in the brain cannot, of course, be remedied by this means, and the method is most valuable in early cases.

Remarkable and long-standing remissions sometimes follow malarial infection, but a genuine restoration to normal is rare, and usually a mild degree of fatuity characterises the patients so treated.

It is generally advisable to conduct the treatment in an institution where any exacerbation of mental disorder can be dealt with adequately.

Tabes Dorsalis.—*Symptomatic Treatment.*—Special symptoms which call for treatment are :—

(*a*) *Ataxy.*—The most striking results are obtained in very many cases by re-educative exercises. In severe ataxia these may be begun in bed, the patient carrying out simple graded movements on the lines described by Fraenkel. Later, carefully graded walking exercises are given on a floor or strip of canvas on which lines or footprints are painted. These exercises demand the full attention of the patient, and at the beginning some skilled instruction. The improvement sometimes reaches restoration of normal co-ordination, which may be maintained for a period of years. In this connection may be mentioned the great importance of keeping tabetics on their feet and the danger of confining them to bed unless it be imperative.

(*b*) *Pain.*—The lightning pains may be controlled or relieved in most instances by aspirin, phenacetin, tincture of gelsemium, and other analgesic

drugs. Morphia is strongly contraindicated unless its use is imperative as a temporary measure. The injection of 60,000 units of penicillin thrice daily for four days is said to afford relief to lightning pains.

(*c*) *Gastric Crises.*—These are often very resistant to palliative treatment. Tincture of iodine in 2-minim doses in water, 5 minims dilute hydrocyanic acid in 2 drachms of water, or chloretone (three or four 10-gr. doses, at six- or eight-hourly intervals) may give relief. Here, also, morphia should be avoided, if possible, on account of the liability to addiction.

(*d*) *Disturbances of Micturition.*—Since there is commonly residual urine in cases presenting these symptoms, infection is a complication which arises sooner or later in most cases, and may require the usual treatment of cystitis. The presence of cystitis undoubtedly aggravates the pains and other disabilities of tabes, and much relief may be obtained by careful attention to the condition of the bladder in this respect.

A regular action of both bowel and bladder is important. The patient should be urged to take exercise within the limits of fatigue, when possible. The presence of perforating ulcer or of joint lesions calls for the rest of the affected part, and in the latter case splinting may be necessary. The majority of tabetic patients are thin and cachectic and their adequate nourishment calls for attention.

EPILEPSY

Epilepsy is a chronic malady characterised by the recurrence of sudden brief disturbances of cerebral function, of which the essential feature is a partial or complete loss of consciousness. To this, in many instances, may be added convulsive movements of varying severity and extent. Momentary attacks with minimal or no convulsive phenomena are spoken of as *petit mal* or minor epilepsy, and more severe attacks with generalised convulsions as *grand mal* or major epilepsy.

Ætiology.—Nothing is known of the causation of epilepsy nor of the essential pathological process in the brain underlying the production of the fits. The fit has no known morbid anatomy, and no constant abnormality of metabolism or of endocrine function has been found in association with it. On the cerebral process which accompanies the fit some light has recently been thrown by the study of the action currents (Berger rhythm, cortical potentials) produced by the nerve cells of the cerebral cortex. By the use of electrodes attached to the scalp and a suitable amplifier, these potentials can be recorded as a wave-like record on paper, somewhat in the manner that the electro-cardiograph records the electrical variations in heart muscle. The pattern of the waves is altered by cerebral activity, and the rhythm is best seen when the subject sits at ease with his eyes closed. In this way the normal range of variations in the record have been established. It is found that during the course of an epileptic seizure, and in epileptic subjects even when no clinically visible fit is present, the pattern is changed in one of three ways. In major fits a fast high-voltage rhythm is seen, in minor fits an alternation of high slow waves and spike-like waves, while in the rarer psychomotor fits another characteristic wave pattern is seen.

While the study of the electro-encephalogram (E.E.G.) may provide confirmatory or excluding evidence of value in doubtful cases of minor epilepsy, it should be remembered that the records call for skilled inter-

pretation, and that wave patterns like those of epilepsy are to be found in some 10 per cent. of the population: that is, in many persons who are not subject to epilepsy, epileptics forming but 0·5 per cent. of the population. Further, it has recently been estimated that in 40 per cent. of clinically diagnosed cases of epilepsy the E.E.G. provides no confirmatory information, while, finally, abnormalities of rhythm are to be found in various organic diseases of the brain. A diagnosis of epilepsy cannot be made on the E.E.G. alone in the absence of clinical evidence. That these electro-encephalographic findings stand in a causal relation to fits is not yet established.

Since fits clinically indistinguishable from those of epilepsy, as we have defined it above, may occur as symptoms in other maladies, it has been suggested that epilepsy is not a distinct disease but a group of allied symptom-complexes expressive of diverse pathological processes to which the term "the epilepsies" might more accurately be applied.

Nevertheless no malady has a more striking and clear-cut clinical individuality, and even though its causation be obscure, few are better entitled to rank as distinct diseases.

Direct inheritance of the disease, though commonly believed to be frequent, is in fact exceptional. If anything be inherited it is no more than a cortical instability that may during life issue in fits, either for no discoverable cause, as in idiopathic epilepsy, or in the presence of such adventitious factors as new growth, inflammation, degeneration, or injury of the brain. A neuropathic inheritance is also thought to be common, and the occurrence of migraine, alcoholism, insanity, and so on in the ascendants is often cited, but these are vague considerations and there is no conclusive evidence of a true inheritance of epilepsy obeying any known laws of inheritance. Syphilis plays no part in its production. The first and second decades of life, especially the latter, are those in which it most frequently begins. Its onset after the third decade is relatively uncommon, and fits beginning later than this should give rise to the suspicion of focal disease. In an epileptic subject fits may be precipitated by various factors such as anxiety, fatigue, gastro-intestinal disturbances, and unhygienic conditions of life.

Symptomatology.—In the case of a major fit the course of events is relatively constant. A momentary subjective sensory disturbance (the aura) may warn the subject of the impending fit. He then falls unconscious, sometimes with a cry. The skeletal musculature at once goes into strong tonic spasm, and when this is unequal on the two sides the eyes and then the head deviate to one side. Sometimes the trunk follows, and occasionally the patient rolls over on to his face, and may thus run the risk of suffocation if he be in bed. The arms are commonly flexed, the legs extended. In a varying number of seconds the tonic spasm begins to intermit, the intermissions rapidly increasing in degree and duration, so that the spasm now becomes clonic in character. The limbs now are the seat of powerful jerking movements. The tongue may be bitten either in the tonic or the clonic stage. Froth is expelled from the mouth with each expiratory jerk, and is blood-stained if the tongue or cheek has been bitten. Cyanosis, due to respiratory spasm, passes off with the resumption of thoracic movement. Evacuation of bladder or rectum may occur. Following the spasm the patient relaxes into a state of flaccid coma, from which after some few minutes he awakes, only to fall into a deep sleep in many instances. Early in the fit the pupils dilate and remain dilated, and the tendon jerks are lost until consciousness is restored. During this time,

also, the plantar responses are found to be of the extensor type. The pulse increases in force and frequency during the period of spasm, becoming transiently feeble as the fit terminates. Headache and sickness may follow the fit.

The *Aura*, or warning, which precedes the fit is present in about three-fifths of all cases of epilepsy, and even when it is not entirely sensory in character has a sensory component. The sensory aura may consist of a vague visceral sensation commonly localised in the epigastrium, the so-called epigastric aura ; or of unilateral or bilateral paræsthesiæ referred to the limbs, trunk, or head ; or of a special sense disturbance, visual, auditory, or olfactory ; or finally, it may be psychical in character such as a passing idea or emotion. Motor phenomena may accompany sensory auras, such as the movement of a limb, a rotation of the head and eyes, jerking or starting movements. They are invariably very brief in duration and are followed instantly by loss of consciousness. Unilateral and localised warnings, sensory, or sensory and motor combined, and special sense warnings (lights, smell, or taste), are of importance as indicating the focus in which the discharge is beginning, and are particularly common in the case of fits arising from local lesions such as tumours.

Sometimes warnings occur which are not followed by fits in the subjects of epilepsy.

The nature and sequence of the convulsive phenomena have already been described. The coma which ensues after cessation of the convulsion may be transitory and rapidly recovered from, or may be prolonged and gradually pass off. In status epilepticus, when fits follow in rapid succession, convulsion may succeed convulsion without any intervening return of consciousness.

On regaining consciousness the patient is unaware of what has happened, except from the circumstances in which he may find himself. Thus the subject of exclusively nocturnal fits may know of the occurrence of a fit during the night only by the fact that he has been incontinent, and that the bed-clothes are disordered.

There is frequently an abundant secretion of urine after a fit, and a trace of albumin or sugar may be present. Occasionally a slight rise of temperature may follow a fit, and in the case of status epilepticus, hyperpyrexia may develop.

In the case of a minor fit the whole attack may consist in nothing more than a momentary blunting of consciousness, which is spoken of by the patient and his friends as a " dizzy turn," a " faint," or a " sensation." Those gazing at the subject when this occurs note a transient vacancy of expression, a little deviation of the eyes, possibly a slight movement of the lips or eyelids or of the head. A transient flush or pallor may pass over the face. The patient ceases whatever he may be doing at the moment of onset, stops talking or moving, or drops something he happens to be holding in his hand. The attack passed off, he resumes his conversation where he left off. In more severe minor attacks consciousness may be completely lost for a moment and the patient falls down, only to pick himself up immediately. A definite slight convulsive movement of the face or of one or both arms may occur. When sitting at table the patient's head may suddenly drop forwards on to the table, only to be raised again instantly. The use of the term " pyknolepsy " to refer to very numerous minor fits in children should be abandoned as it involves no real distinction from minor epilepsy.

Even in the absence of any trace of convulsion some subjects of minor epilepsy pass urine involuntarily in their fits.

The frequency of fits varies greatly from case to case. In minor epilepsy numerous daily attacks may occur, or, on the other hand, intervals of days or even weeks may separate the fits. In the case of major fits, also, almost daily attacks or fits separated by periods of months may be the rule. In some epileptics major attacks occur only during sleep or at some other special time, as just after waking in the morning. Fits of both types are frequently present in the same subject, the appearance of major attacks being preceded for some years by minor fits. In women the menstrual period is often accompanied by a special incidence of attacks.

Other phenomena found in association with epilepsy are post-epileptic automatism, post-epileptic hysteria, and mental deterioration.

In post-epileptic automatism the subject immediately after the cessation of the attack, most commonly a minor fit, carries out some complicated act, such as removing some particular article of clothing, undressing, wandering from the house, or becoming violent. In a given subject the form of the automatism tends to be constant, and when he finally comes to normal consciousness he is completely unaware of what has passed. Since such behaviour may follow a momentary and unnoticed minor fit, various social and legal complications may arise when the automatic behaviour assumes certain forms.

Again, an hysterical fit or some emotional manifestation may follow a minor or major attack, and give rise to a diagnosis of hysteria in the subject of epilepsy. In all such cases a careful inquiry into the history and into the period immediately preceding the alleged hysterical phenomena may reveal the real nature of the situation.

Mental deterioration sometimes develops in the subjects of repeated fits of either type. This is the greater when fits are numerous and the malady of long standing; for example, in subjects who have been affected since childhood, and particularly in the case of minor attacks of great frequency. In these circumstances the epileptic child may become intractable, spiteful, untruthful, and quarrelsome. After many years of major attacks, a slowly progressive dementia may set in. It must be remembered, however, that these changes are not constant even in severe cases of the disease.

Prognosis.—With each fit the liability to further attacks tends to increase, and the spontaneous cure of epilepsy is extremely rare. There is no foundation for the widespread belief that fits beginning in infancy often cease to occur after puberty, or that the age of twenty-one is a period when spontaneous cure may be looked for. Prognosis depends, therefore, upon the effectiveness and continuity of treatment. Marriage and pregnancy have no definite influence upon the course of the disease. A fatal termination to a single fit is exceptional, and when it occurs is due to some such complication as injury, drowning, or asphyxia during the period of coma. In status epilepticus death may ensue from exhaustion, but this is uncommon.

Diagnosis.—In idiopathic epilepsy diagnosis commonly depends upon an accurate history, since physical examination reveals no objective abnormalities due to the disease. It would be an error to suppose that an electro-encephalogram is necessary for the diagnosis of epilepsy, or that this diagnosis can be made on the basis of this instrumental procedure in the absence of adequate clinical evidence. In exceptional and obscure cases of

suspected minor epilepsy it may happen that the electro-encephalogram gives supporting evidence, but even here it is not yet infallible and a final balance of opinion as to its value has yet to be reached. Further, as has been stated earlier, fits indistinguishable from those of idiopathic epilepsy may occur as symptoms of a variety of pathological conditions : intracranial tumour, general paralysis, intracranial hæmorrhage and thrombosis, cardiac and renal disease.

It is especially when fits make their first appearance after the age of thirty years that evidence of one or other of these conditions should be sought for before a diagnosis of epilepsy is made. In all but one of them such evidence may be found, but as has been emphasised on page 582, generalised fits may be the first indication of the growth of an intracranial tumour. Attacks of transient unconsciousness due to heart block (Stokes-Adams syndrome, *vide* p. 382) may sometimes be mistaken for epilepsy. If the patient be seen in an attack the extreme bradycardia will settle the diagnosis.

In differentiating an epileptic from an hysterical fit it must be remembered that there is a constant sequence of events in the former, but that in the latter every patient is a law unto himself. The convulsive movements of epilepsy are clonic jerking movements ; those of hysteria are complex disorderly movements of infinite variety, which tend to increase in force and extravagance if the patient be restrained. Hysterical fits do not occur during sleep, in dangerous situations, nor except in the presence of an audience. The reflexes, pupillary, corneal, and tendon, are all retained during an hysterical fit, and tongue biting and incontinence do not occur.

Treatment.—The maintenance of a high level of general health and of a healthy regime of life are essential. Pressure of work or, in the case of children, of education and stress of any kind are unfavourable, and tend to nullify the effects of drug treatment.

A daily regular action of the bowels is of importance, and if there be difficulty in this respect it is best to remedy it as far as possible by diet rather than by the habitual use of aperients. These, however, may be essential. An open-air life is best when practicable. Alcohol is contraindicated.

The general statement may be made that minor epilepsy is more difficult to control than major. In cases that respond well to moderate doses of bromide, that are not of long standing, and in which the fits are relatively infrequent, freedom from fits is often obtained.

Whatever drug or combination of drugs be adopted in any given case, the essential condition of success is continuity of treatment. No drug has an influence for more than a few hours after administration, and the intermittent administration of drugs, or their omission on the specious plea that they impair the intellectual energy of the patient, as soon as freedom from fits for a few weeks or months has been achieved, are absolutely unjustifiable. The sudden cessation of repeated fits is sometimes followed by a period of depression, which is apt to be attributed to the drug used. When depression can reasonably be ascribed to this cause, the proper remedy is not the abandonment of treatment but a change of the drug. The successful treatment of any given case is a matter of trial and error, and many changes may be necessary before the best possible results are obtained.

Of the various drugs of value those longest in use are the bromides of sodium or potassium. The dose used and the time of administration vary with each case. In nocturnal epilepsy a single daily dose of from 10 to 30 gr. may

be given at bedtime. In other cases two or three daily doses may be given. Another valuable adjuvant is tincture of belladonna (10 minims). It is well borne by children, and sometimes the dose may be increased to 15 minims with excellent results.

Of recent years phenobarbitone (luminal) has been extensively used. Sometimes phenobarbitone may usefully be combined with moderate doses of bromide and belladonna. Not more than ½ gr. phenobarbitone should be given in a single dose until the patient's tolerance is ascertained. The common signs of intolerance are dizziness, drowsiness, and the appearance of erythematous rashes. Recently a substance known as sodium diphenyl hydantoinate (Epanutin, Solantoin) has been introduced, and in some cases it has proved more effective than the remedies already available. The dose is 1½ gr. three or four times daily for an adult and half that dose for a child. When used to replace phenobarbitone the change-over should be made gradually over a period of two weeks. No final judgment is yet possible as to the usefulness of Epanutin, and at present it is best used in those cases which have not responded satisfactorily to better-known remedies, or in combination with phenobarbitone. In a few patients toxic symptoms follow its administration. These include nausea, tremor, dizziness, and even diplopia, while in severe cases of intolerance a purpuric dermatitis may ensue. Prolonged administration is not rarely followed by a high degree of hyperplasia of the gums.

When fits are known to occur at certain special periods, as before menstruation, the use of an aperient and an increase of the dose of drug used may fend off attacks.

During the course of a major fit the handle of a spoon or tooth-brush introduced between the teeth may prevent tongue-biting. The patient is best kept flat on his back, with collar loosened. To arrest the course of status epilepticus, hyoscine hydrobromide ($\frac{1}{200}$ to $\frac{1}{100}$ gr.) or morphine (¼ to ½ gr.) may be given hypodermically, or paraldehyde (4 drachms) per rectum.

In an ordinary case of epilepsy *it is never safe to discontinue the use of drugs until there has been no fit for three years*, although after the second year the dosage may be progressively diminished. While psychotherapy may be of value in remedying any maladaptation to his environment which the patient may show, it can never be more than an adjuvant to continuous drug medication. Experience shows that few common maladies are less efficiently treated, in general, than epilepsy. Despite the advice, reiterated in every textbook, that there is no short cure and that long-continued medication is essential, it is distressingly common to encounter patients who have never been made aware of this necessity by their medical advisors, and indeed have been encouraged by them to abandon treatment within a few months of the cessation of fits. No one can foretell of any patient that medication will render him free from liability to recurrent fits, but not a few are made free when treatment is kept up without interruption for an adequate period. On the other hand, it may confidently be stated that short-term or irregular medication will never lead to a permanent cessation of fits. The carelessness of patients, their parents, and relatives is often responsible for ineffective medication, but it cannot be denied that erroneous views on this matter held by their medical advisers are not less frequently to blame.

NARCOLEPSY

Narcolepsy is a rare condition in which the patient is periodically overcome by an irresistible desire for sleep. He can be aroused, but if left undisturbed may slumber for as long as half an hour, awaking to normal consciousness. Such accesses of somnolence may occur several times daily. Associated with these is a phenomenon of another order. Whenever the patient feels the impulse either to laughter or to anger, a sudden weakness overcomes him and he sinks helpless to the ground, retaining full consciousness and recovering in a few seconds. This is known as cataplexy.

The causation of the condition is unknown and the patient is otherwise healthy.

A few cases of narcolepsy are found to respond favourably to ephedrine sulphate in $\frac{1}{2}$-gr. doses twice or thrice daily, but really remarkable results have been obtained by the administration of benzedrine sulphate (benzyl-methylcarbinamine sulphate) in doses of from 10 to 30 mg. twice daily, preferably on rising and at midday. The larger dose should be used with caution, symptoms of overdosage being excitability, dilated pupils, and inability to relax.

MIGRAINE (PAROXYSMAL HEADACHE)

A paroxysmal nervous disturbance of which the most constant feature is headache. This may be the sole feature, but in the fully developed attack visual and other sensory phenomena may be present, and also nausea with or without vomiting. This association of gastric symptoms leads to the names " sick headache " and " bilious headache " by which the affection is widely known.

Ætiology.—The condition commonly begins in childhood or adolescence, and the subject remains liable to attacks until past middle age. Females are more frequently affected than males. Direct inheritance can be traced in most cases, and evidence of a neuropathic heredity is not uncommon. Of predisposing factors, errors of refraction are regarded by some as of primary importance but they are not constantly present, and when present their correction does not invariably give relief. Other factors of this order are fatigue, worry, and gastro-intestinal disturbances.

Symptomatology.—On the day preceding an attack the patient may suffer from a vague malaise which warns him to expect it. When, as is frequently the case, the attack consists of headache alone, the subject awakes in the morning with unilateral headache, commonly temporal. This waxes in intensity and becomes severe, being aggravated by movement, strong light, and noise. It is least intense in the recumbent posture. It is boring and throbbing in character and may become bilateral when at its maximum. There is seldom any superficial tenderness, but eye movements, especially lateral deviation, or pressure on the globes may be slightly painful. Nausea frequently follows the onset of the headache. If the subject is able to keep completely at rest, the headache may pass off in an hour or two, but otherwise it usually persists all day.

In a fully developed attack other and more striking symptoms are added

to these, and the characteristic sequence of events is as follows: The patient is suddenly conscious of a bright illuminated and shimmering spot on one side of the field of vision. This tends to enlarge and to open out into a curved zigzag figure, the so-called "fortification spectrum." This figure flickers before him and may be accompanied by a blotting out of part of the field of vision, which sometimes amounts to a hemianopia. Occasionally the visual defect exists without the figure. Accompanying these phenomena some patients may experience a tingling sensation in the tongue, which may also extend to the lips and fingers. In some cases a transient disturbance of speech of true aphasic character may occur. This group of symptoms endures for from ten to twenty minutes, then ceases, and is at once replaced by unilateral headache of the type already described, by nausea, and frequently by vomiting. The vomiting may herald the end of the attack, which may be followed by a copious secretion of urine.

Sometimes the sensory phenomena of migraine occur without being followed by headache.

The paroxysms occur at varying intervals, from once or twice a week in severe cases to attacks every few months.

Diagnosis.—The definite paroxysmal course, the sensory accompaniments, the unilateral character of the headache, and the absence of objective signs of disease serve to differentiate migraine from other forms of headache.

In those cases with marked sensory symptoms a diagnosis of minor epilepsy is sometimes made. In minor epilepsy, with visual and other forms of sensory aura, the duration of the aura is momentary, lasting a few seconds. In migraine the sensory symptoms last for as long as twenty minutes and are immediately followed by the characteristic headache and nausea. In epilepsy, also, a definite fortification spectrum is not present.

Treatment.—The avoidance of precipitating factors must be attempted, be these fatigue, dietary indiscretion, or any local disturbance of health. Any error of refraction that may be present should be corrected. Drug treatment consists in the continued administration of drugs to prevent the occurrence of attacks and the relief of the attack when it has appeared. For the former purpose the continuous use of bromide with nitroglycerin is generally of definite value, and the following prescription has the sanction of long and successful use: sodii bromide., gr. x; liq. trinitrin, ℥i; liq. strych., ℥iv; acid hydrobrom. dil., ℥x; tr. gelsem., ℥x (aquam., ad ℥ss), t.d.s. Ergotamine tartrate may avert an impending or cut short a developing attack. It may be given hypodermically (0·5 c.c. of a 0·5 per cent. solution) or by mouth ($\frac{1}{60}$ to $\frac{1}{30}$ gr.). It is not suitable for regular medication and makes some subjects very sick. Luminal in small doses ($\frac{1}{4}$ to $\frac{1}{2}$ gr. t.i.d.) has also been recommended. When the attack has developed, rest in the dark and the administration of such a powder as the following may be of use: aspirin, gr. v; phenacetin, gr. v; caffeine, gr. i. Occasionally alcohol or even food may have a beneficial effect in cutting an attack short, or a 50-mg. dose of nicotinic acid.

AFFECTIONS OF THE CRANIAL NERVES

Lesions of the cranial nerves or of their immediate central connections occur in association with various more extensive diseases of the nervous system. In this chapter we shall deal briefly with the signs of involvement of

the different cranial nerves, and also with certain symptom-complexes wholly or in large degree expressed by disordered function of these nerves.

The Olfactory Nerve

This nerve subserves the sense of smell, which includes the appreciation of both odours and flavours. The true gustatory apparatus deals only with sensations of sweetness, sourness, saltness, and bitterness, which make up but a part of the range of what is commonly regarded as "taste." It is frequently by his diminished appreciation of the savour of his food that the subject of anosmia becomes aware of his disability. Lesions of the cerebral olfactory centres in the temporo-sphenoidal lobe do not produce anosmia, but subjective sensations of smell may be a feature of Jacksonian fits arising here.

Bilateral anosmia may arise from local disease in the nose, and its presence, therefore, has not necessarily any value in neurological diagnosis. Both bilateral and unilateral anosmia may result from the pressure of frontal lobe tumours upon the olfactory bulbs, while anosmia is a common and sometimes the only permanent objective sign of fracture of the base of the skull—an injury in which the olfactory filaments may be torn from the bulb.

The Optic Nerve

Anatomy.—After leaving the orbit the optic nerve meets its fellow at the optic chiasma, where a partial decussation takes place. The fibres from the nasal halves of the retinæ decussate, but those from the temporal halves enter the optic tract of the same side uncrossed. The optic tracts pass backwards from the optic chiasma round the midbrain and each contains fibres from the temporal half of the homolateral retina and from the nasal half of the other retina. Owing to this semi-decussation lesions of the chiasma abolish the functions of the nasal half of each retina and thus produce bitemporal hemianopia. Lesions of one optic tract, on the other hand, produce homonymous hemianopia : blindness of the nasal field on the side of the lesion and of the temporal field on the opposite side. Each optic tract passes backwards and, bending round the lateral aspect of the midbrain, reaches the lateral geniculate body where the majority of its fibres end. The optic radiations arise in the geniculate body, which is the primary optic centre, and pass to the visual cortex. Other fibres in the optic tracts pass to the superior quadrigeminal bodies. These fibres are not visual in function but are concerned in reflex pupillary reactions to light and to accommodation. Owing to the involvement of these fibres in optic tract and nerve lesions the visual disturbance may be associated with alteration of the pupillary reactions. Thus blindness due to a complete lesion of the optic nerve is associated with a large immobile pupil, while in optic tract lesions the illumination of the blind field of the retina does not provoke a light reaction (Wernicke's hemianopic pupil reaction).

It is interesting to note here that hemianopia or blindness, associated with lesions of one or both visual regions of the cortex respectively, is not accompanied by loss of pupillary light reaction—a point of some importance in the localising diagnosis of lesions of the visual system (*vide* Fig. 27).

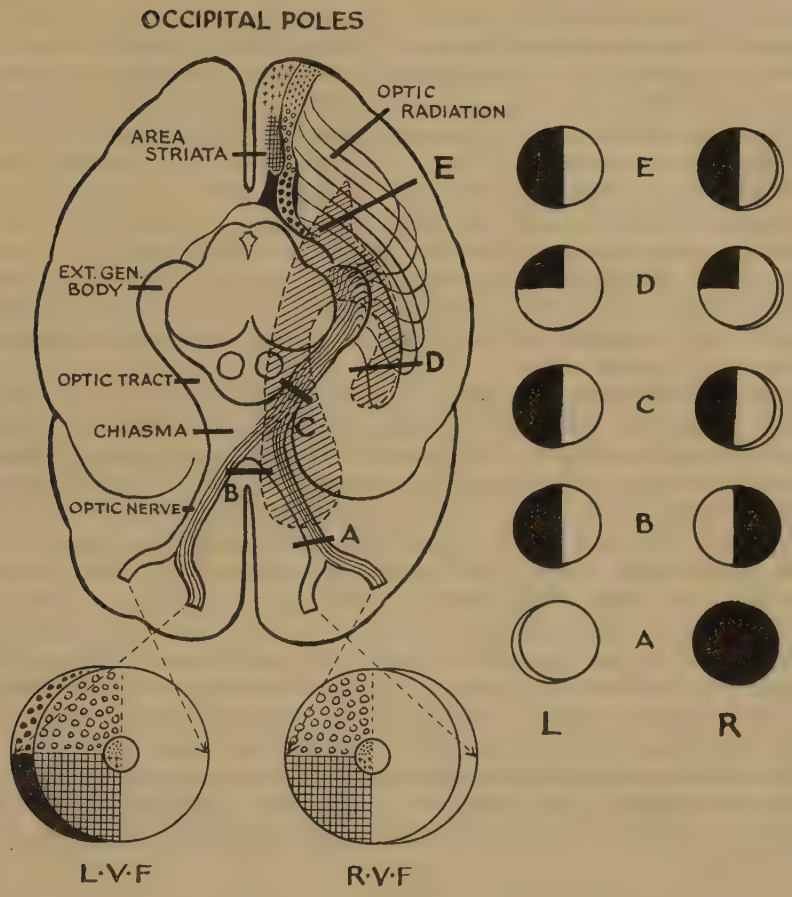

FIG. 27

THE VISUAL PATHWAYS

The course of the visual fibres from the right homonymous halves of the two retinæ to the right occipital pole is represented. The termination of the right optic tract in the external geniculate body can be seen and also the course of the optic radiation to the area striata surrounding the calcarine fissure. The relation of the radiation to the descending horn of the lateral ventricle in the temporo-sphenoidal lobe is indicated, the most anterior part of the radiation being the so-called temporal loop. The topographical representation of the different parts of the visual field in the area striata can be seen. On the right of this anatomical diagram are represented the disturbances of the visual field resulting from lesions at different parts of the visual pathway.

A, Lesion of the right optic nerve, resulting in complete blindness of the right eye with immobility of the pupil.
B, Lesion of the anterior border of the chiasma, resulting in bitemporal hemianopia.
C, Lesion of the optic tract involving loss of vision in the left homonymous half-fields.
D, Lesion in the temporo-sphenoidal lobe, involving the temporal loop of the optic radiation and producing loss of vision in the left homonymous upper quadrants of the half-fields.
E, Lesion of the optic radiation leading to a left homonymous hemianopia.

(Modified from Bender and Kanzer.)

Many affections of the optic nerve within the eye do not come in question here, such as neuroretinitis or papillœdema from raised intracranial tension.

The optic nerve may be damaged in fractures of the middle fossa of the skull which extend to the optic foramen. Sudden and complete blindness and subsequent primary optic atrophy result from such an injury. Tumours in or above the sella turcica may compress the nerve or chiasma and produce the visual disturbances described in the chapter on Intracranial Tumours. The visible result of this compression is primary optic atrophy. Tumours of the temporo-sphenoidal lobe may press mesially upon the optic tract and produce the visual and pupillary symptoms described above.

Symptoms.—The clinical manifestations of lesions of the optic nerve are (i) impairment or loss of vision over part or all of the visual field ; (ii) impairment or abolition of the pupillary light reaction ; (iii) visible changes in the appearance of the optic disc.

Retrobulbar Neuritis.—Localised lesions of the optic nerve may arise from a variety of causes. The pathological process tends to arise and be most severe in the deep central part of the nerve, with the result that the characteristic visual disturbance is a central scotoma in the field of vision. There is also impaired mobility of the pupil on illumination. If the lesion be close behind the eye there may be some swelling of the disc amounting sometimes to a definite papillœdema. In other cases no abnormality is seen in the disc during the acute stage of the lesion, but at a varying period of weeks subsequently pallor of the disc appears and a varying degree of primary optic atrophy. The various causes of retrobulbar neuritis are *toxic* : excessive consumption of tobacco produces a recoverable retrobulbar neuritis manifested by a central scotoma. Methyl alcohol may lead to a rapidly developing neuritis with blindness and optic atrophy. *Disseminated sclerosis* is the commonest cause of retrobulbar neuritis in otherwise healthy young adults, women particularly. The symptoms have been described in the chapter dealing with this disease (*vide* p. 619, also Neuromyelitis Optica, p. 622.)

The Oculomotor Nerves : Third, Fourth, and Sixth

The cells of origin of these nerves lie in the grey matter close to the middle line in series from before backwards, the third and fourth nerve nuclei in the midbrain, and the sixth in the pons. The fibres of the third and sixth pass ventrally to emerge on the under surface of the brain stem at the anterior and posterior ends of the pons respectively, while those of the fourth pass dorsally, decussate, and emerge on the dorsal aspect of the brain stem posterior to the posterior corpus quadrigeminum.

The third nerve supplies (i) the internal (medial), superior, and inferior recti, the inferior oblique and levator palpebræ superioris ; and (ii) the ciliary muscle and the sphincter pupillæ. The fourth nerve supplies the superior oblique muscle. The sixth nerve supplies the external (lateral) rectus muscle.

General Symptoms of Ocular Paralysis.—Loss of power in ocular muscles produces limitation of movement of the eyes, non-correspondence of the visual axes (*i.e.*, squint), diplopia, secondary deviation of the sound eye, and erroneous projection. The limitation of movement is in the direction of the weak or paralysed muscle, and as a consequence ocular movements employing a paralysed muscle result in squint. This squint is due not only to failure

of the affected eye to make a normal excursion, but also to a secondary deviation of the sound eye—that is, an excessive movement of the sound eye in the desired direction, the result of the extreme effort made to swing the weak eye to the required position. A further result of the secondary deviation of the sound eye is erroneous projection of the visual image. This arises as follows : The increased effort at innervation of the weak eye corresponds to a greater degree of movement than is actually taking place, and the image tends to be projected in space to the point at which the degree of effort made corresponds when ocular movement is normal. Thus the image is projected in the direction in which the eye is unable to move, and farther in that direction than the object actually is. Erroneous projection is always most pronounced when the affected eye alone is being used and is not present when only the normal eye is in use. The diplopia, or double vision, results from the non-parallelism of the optic axes.

Lesions of the Third Nerve produce, when complete, loss of all ocular movement except outward movement (which is intact) and slight downward and inward movement. Diplopia is present in all movements involving the paralysed muscles. There is complete ptosis with an associated compensatory overaction of frontalis and elevation of the eyebrow, and dilatation with immobility of the pupil and ciliary paralysis with loss of accommodation. Partial lesions are common, and in these circumstances the various extrinsic muscles are very unequally affected, and the intrinsic muscles may escape or vice versa.

Lesions of the Fourth Nerve are rare apart from associated lesions of the third or sixth, but when isolated produce diplopia in all directions when the gaze is directed below the horizontal. The patient inclines the head downwards and towards the sound side. There is a very slight convergent squint.

Lesions of the Sixth Nerve produce loss of outward movement with convergent squint and diplopia. The two images are parallel and uncrossed.

Abnormalities of Pupillary Action.—The size and reactions of the pupil depend on the action of the circular muscle fibres (sphincter pupillæ) which are innervated by the third nerve, and of the radiating fibres which are innervated by the sympathetic. The iris has three actions : (i) reflex contraction of the sphincter to light ; (ii) reflex contraction of the dilator fibres on cutaneous stimulation ; and (iii) contraction of the sphincter, in association with contraction of the ciliary muscle, on accommodation.

The anomalies of pupillary reaction which may occur are : (i) paralysis of accommodation—the pupil does not contract on accommodation ; as a result near vision is blurred. (ii) Loss of the light reflex ; since both eyes react to illumination of one, each eye must be tested separately in a strong diffuse light.

In third nerve lesions with associated sympathetic paralysis the pupil is of moderate size and completely immobile. In isolated sympathetic paralysis the pupil is small, there is apparent enophthalmos (from paralysis of orbital muscle), and narrowing of the palpebral fissure from paralysis of the smooth muscle fibres in levator palpebræ superioris (Horner's syndrome).

Loss of the light reflex may occur as an isolated phenomenon, but is usually associated with myosis and irregularity and inequality of the pupils.

Tonic Pupil.—A rare condition has been described by this name. One or both eyes may be affected. The pupil is of normal size, or larger than its fellow when this is not affected. It does not respond to light, and its response

on convergence is very slow. The patient is commonly a healthy young woman, but sometimes this phenomenon is accompanied by a complete absence of tendon jerks. Whether it occurs alone or with this loss of reflexes. the condition is not syphilitic in origin and is not related to tabes dorsalis. Occasionally, when the pupil affection is unilateral, the patient may complain of some blurring of near vision. Otherwise the condition is symptomless and of no practical significance, but it is important not to confuse it with tabes dorsalis.

Compound and Nuclear Ocular Paralysis.—Loss of convergence and of accommodation, when lateral eye movement is intact, is a rare result of a nuclear lesion. Loss of vertical movement with paralysis of the levators is a common sequel of midbrain lesions involving the supranuclear mechanisms for ocular movement. Loss of conjugate deviation of the eyes is a transient result of cerebral lesions, and may also occur in pontine lesions.

Ætiology of Ocular Paralyses.—Ocular paralyses may be due to peripheral lesions of the oculomotor nerves, in the orbit or in their intracranial course, or to central lesions involving the nerve fibres, the nuclei, or the supranuclear co-ordinating centres in the midbrain and pons.

Peripheral Lesions may be due to injury—that is, to fractures involving the walls of the orbit or the middle fossa of the skull, or sometimes to blows without fracture. The lesion is usually unilateral and may affect one or more of the nerves. A form of neuritis of the oculomotor nerves allied to the familiar Bell's palsy occasionally occurs. It may be associated with fifth nerve involvement. It is acute in onset, accompanied by severe pain in the face and in the eye itself, and with paralysis of one or more ocular muscles. Periostitis of the bones entering into the sphenoidal (superior orbital) fissure has been suggested as the cause of the condition. Within the skull a meningitic process is usually in question, and syphilis is by far the commonest cause of paralysis of oculomotor nerves in this situation. Other lesions are tumours of the base of the skull, chiasmal tumours, carotid aneurysm (perhaps the commonest cause of isolated and unilateral third nerve palsy), cavernous sinus thrombosis, and subarachnoid hæmorrhage. Occasionally, isolated sixth nerve paralysis occurs in elderly subjects for no discoverable reason, but may possibly be due to pressure on the nerve of a distorted atheromatous carotid artery. In association with acute mastoid disease in children the development of severe neuralgic pain in the side of the head and face may be followed by a sixth-nerve paralysis with squint and diplopia. This is known as "Gradenigo's syndrome" and has already been referred to (p. 588). It is thought to be due to a localised meningitis at the tip of the petrous bone where fifth and sixth nerves lie in close proximity. Recovery is the rule, though surgical treatment of the mastoid disease may first be required.

Central Lesions arise in a variety of conditions, including disseminated sclerosis, lethargic encephalitis, focal lesions of whatever nature in pons or midbrain, diphtheria (accommodation paralysis), and in the so-called ophthalmoplegic migraine. With lesions in this situation the paralyses may be nuclear or supranuclear in character. Ocular paralyses of both peripheral and central types may be seen in tabes dorsalis, while pupillary abnormalities (Argyll-Robertson pupil), myosis, irregularity, and inequality may occur in all forms of neurosyphilis.

In rare instances a chronic nuclear ophthalmoplegia is associated with chronic bulbar palsy or progressive muscular atrophy.

The Trigeminal Nerve

Anatomy.—This is the largest of the cranial nerves. It has motor and sensory roots, and on the latter is the Gasserian (trigeminal) ganglion. The larger sensory division supplies sensory fibres to the anterior part of the scalp, eyes, nose, mouth, and parts of the ear and tongue, as well as the dura mater. The motor portion supplies the masticatory muscles. The cells of origin of the motor root lie beneath the floor of the fourth ventricle in the upper part of the pons. The larger sensory portion sends its fibres into a long column of cells which extends caudally as far as the third cervical segment of the cord and lies at the tip of the posterior horn in the substantia gelatinosa Rolandi, and in the medulla lies in the lateral portion. It also extends forward into the pons close to the motor nucleus. The motor and sensory roots leave the pons on its anterolateral surface side by side in a sheath of dura mater known as the cavum Meckelii (cavum trigeminale), on the tip of the petrous portion of the temporal bone. Here the sensory root enters the Gasserian ganglion, from which emerge the three sensory divisions of the nerve : the ophthalmic, which enters the orbit ; the maxillary, which leaves the skull by the foramen rotundum ; and the mandibular, or third division, which leaves the skull by the foramen ovale. The ophthalmic division supplies sensory fibres to the eye, lachrymal gland, the meninges, and the skin of the anterior part of the scalp and of the face above the eye. The maxillary division supplies the skin of the face from the upper lip to the lower eyelid inclusive, and laterally as far as the pinna, the upper jaw and teeth, and the lower part of the nasal cavity.

The mandibular division supplies the side of the face, the pinna and external auditory meatus, the greater part of the tongue, the mucous membrane of the mouth, lower teeth, gums, and Eustachian (pharyngotympanic) tube. The motor root supplies the masseter, temporal, pterygoid, mylohyoid, digastric (anterior belly), tensor palati, and tensor tympani muscles.

Symptomatology.—Lesions of the fifth nerve produce sensory loss and paræsthesiæ within the distribution of the nerve. In slowly progressive lesions the earliest manifestation of sensory change is diminution or loss of the corneal reflex. Severe pain, like that of trigeminal neuralgia, does not accompany gross lesions of the nerve. Wasting and weakness of the muscles named above accompany involvement of the motor root of the nerve. In unilateral lesions the jaw deviates to the side of the lesion, pushed over by the unantagonised external (lateral) pterygoid muscles of the opposite side. Wasting of temporal and masseter muscles is visible, and on clenching the jaw weakness or paralysis of these muscles can be felt on palpation.

Ætiology.—Herpes zoster of the Gasserian (trigeminal) ganglion may produce a herpetic eruption with intense pain over the ophthalmic division. Sensory loss of the cornea leads to intractable ulceration. In its intracranial course the nerve may be involved in any of the processes mentioned in connection with the oculomotor nerves. In tabes dorsalis an area of analgesia over the nose and adjacent skin is common, while in syringomyelia the territory of the fifth nerve may be affected when the spinal root of the nerve is involved in the lesion.

Trigeminal Neuralgia (Tic Douloureux)

Trigeminal neuralgia is a malady of unknown origin and with no discoverable lesion, of which the expression is the occurrence of paroxysms of intense pain in the distribution of one or more divisions of the fifth nerve. It is not comparable with any other variety of neuralgia in that, although it may endure for many years, no structural lesion of the fifth nerve ever develops and no objective clinical signs of impaired function in the nerve appear.

Ætiology.—It is pre-eminently a malady of elderly persons, although it occurs exceptionally in young adults and sometimes in middle-aged persons. The two sexes are equally affected. Nothing is known of any causal factors. Since it may develop in persons who have been completely edentulous for a number of years, septic conditions in the mouth or tooth sockets cannot stand in any essential relation to it. In the subjects of the malady it is prone to appear especially in cold, damp weather, and in the presence of debilitating factors.

Symptomatology.—The symptoms tend to increase steadily in severity over a number of years. At first the periods during which paroxysms occur are comparatively short, amounting to one or two weeks, and are separated by intervals of many months. Later, these periods increase in length and frequency, and ultimately the subject may never be wholly free from pain. Similarly, both the distribution and severity of the pain tend to increase with the passage of years. Occasionally, however, the malady disappears after a few periods of paroxysms.

Of the three divisions of the nerve, the second and third are most frequently affected. It is rare for pain to occur in the distribution of the first division unless it is also present in the other two divisions, but neuralgia confined to either of the two latter may occur. Not only may pain spread over face and scalp, but it may extend down the side of the neck to the region of the shoulder and be present in the gums, tongue, the fauces, and ear.

The pain may be of terrible intensity, and is described as being like "red-hot needles," "lightning stabs," "shoots of pain," and many other descriptive terms are used which indicate both the neuralgic character of the pain and its severity. Each paroxysm begins acutely and consists of a rapid series of pains which wax to a maximum and rapidly wane. It may last for from ten to sixty seconds, and in severe cases is accompanied by free lachrymation and salivation and by reflex twitchings of the face. When the paroxysms are of great frequency, a residual aching pain may bridge the intervals between them, so that the patient is never free from pain. Although during the period in which they are occurring paroxysms may come on spontaneously, yet they are provoked by any movement of the face such as speaking, chewing, or expressional movements. Further, touching the face, or currents of cold air playing upon it, may start a paroxysm. Such patients often are compelled to abstain from shaving or from washing the face or teeth on the affected side for many days, and they remain motionless and in terror of pain for hours at a time.

Pressure over the branches of the nerve at their points of exit from the bone will provoke a paroxysm.

Unilateral furring of the tongue is common when the third division of the nerve is the seat of pain.

No objective physical signs of a lesion of the nerve are to be found. The

corneal reflex is intact, cutaneous sensibility is normal, and the motor division of the nerve is unaffected.

Naturally, depression and debility attend the frequent and persistent occurrence of paroxysms of neuralgia (see also Glossopharyngeal Neuralgia, p. 670).

Diagnosis.—The appearance of the patient during a paroxysm, the history of the illness, and the absence of objective physical signs render diagnosis easy. Gross lesions of the fifth nerve, such as compression by a gummatous meningitis or by a tumour, produce objective signs of impaired activity: loss of the corneal reflex, sensory loss, neuroparalytic keratitis, and also associated signs of involvement of neighbouring nervous structures. They do not produce pain of any severity or in any way resembling that of trigeminal neuralgia.

Treatment.—When a case of the malady comes under observation early in its course it is important to remember that the periods during which paroxysms may be expected to continue is short and may be followed by a long interval, exceeding a year, of complete freedom from pain. This should prevent us from taking steps of a more radical nature than the circumstances demand. In short, many cases of trigeminal neuralgia can be adequately treated over a period of several years by simple drug medication, and do not require any form of surgical procedure be it alcohol injection into the nerve or actual removal of the Gasserian ganglion and its roots.

The drugs most valuable for the purpose are tincture of gelsemium, the bromides, acetyl salicylic acid, and allied substances. A useful combination in cases of some severity is: tincture of gelsemium, ℥x; luminal-sodium, gr. ss; sodium bromide, gr. xv; phenazone, gr. v. If this or some similar combination does not give absolute freedom from pain, it so reduces its intensity as to allow of the proper nutrition and rest of the subject, both of which are essential elements in treatment.

The removal of teeth is usually resorted to, but does not materially relieve the frequency or the intensity of the paroxysms. This question must be considered wholly from the dental point of view, and it is rarely justifiable to remove teeth for no other reason than the relief of pain. In long-standing and severe cases drugs may give no relief, and recourse must then be had to alcohol injection into one or more divisions of the nerve. This is a skilled procedure, and in inexperienced hands may produce serious and untoward effects owing to misdirection of the injecting needle and fluid. The method consists in the introduction of a long needle into the region of the foramen ovale and the injection of 80 per cent. alcohol (10 to 50 minims) into the ganglion or the second and third divisions of the nerve. A successful injection gives complete relief for a period up to two or more years. Final and absolute relief is given by division of the sensory root of the nerve, but permanent anæsthesia of cornea and face on the affected side results.

Facial Hemiatrophy.—This is a rare malady characterised by progressive atrophy of skin, subcutaneous tissues, muscle, and bone within the sensory territory of the trigeminal nerve. There is neither paralysis nor sensory loss in the affected tissues. Its causation and the pathological process responsible for the condition are both unknown. It is more common in females than in males, and develops gradually in early adult life.

The tissue atrophy may extend to the whole area innervated by the trigeminal nerve, or be confined to one or more divisions of this area. It may start in a restricted spot and spread from this. The skin becomes thinned and

pale, the subcutaneous fat disappears, the muscles waste, and then the bony structures of the face gradually shrink, including the alveolar processes of the jaws. The whole affected half of the face is shrunken and unsightly. Diagnosis is simple. The process is not influenced by any known method of treatment.

The Facial Nerve

Facial Palsy: Bell's Palsy.—This is an affection of adult life, and is comparatively rarely seen at an earlier period—apart, of course, from middle ear disease and involvement of the facial nerve in petrous caries. Bell's palsy has been attributed to exposure to cold and to involvement of the facial nerve in cases of geniculate herpes. It certainly appears true that there is a periodicity in the appearance of fresh cases of Bell's palsy—namely, in the late autumn and early spring. This would suggest a common ætiology for all cases. However, as has been mentioned on page 633, not all cases of facial palsy associated with herpes of the external auditory meatus are accompanied by geniculate herpes, though the available pathological evidence does not exclude the possibility that some such cases may be so associated. The ætiology of Bell's palsy, therefore, remains uncertain, but it is probable that in all cases we are dealing with a neuritis of the facial nerve in its intratemporal course.

Symptoms.—The onset of facial paralysis is usually, though not invariably, preceded by pain below and behind the ear and sometimes by tenderness of the sternomastoid muscle at its point of insertion. Occasionally a large and tender gland may be palpable in the angle between jaw and mastoid. The paralysis is usually sudden in onset and complete at once, but a few cases are seen in which total palsy is not present for from twenty-four to thirty-six hours.

All the muscles of the affected half of the face, including the platysma, are flaccid and toneless. The face is manifestly asymmetrical even when at rest and the affected half seems to sag. Tears trickle over the margin of the lower eyelid and saliva from the angle of the mouth.

When the patient attempts to close his eye the upper lid descends somewhat owing to reciprocal inhibition of levator palpebræ superioris and the eye rolls up. This upward movement of the eye exceeds the normal upward movement of the eye on the opposite side, and is an overaction strictly comparable with the secondary deviation of the sound eye which we met in the case of ocular palsies (p. 658).

The patient cannot whistle or blow out his cheek; on drinking, fluids tend to trickle out from the angle of the mouth and solid food to collect within the flaccid and paralysed cheek. Taste is lost over the anterior two-thirds of the tongue if the nerve is affected between the geniculate ganglion and the distal point at which the chorda tympani leaves the nerve. The stapedius muscle is also paralysed, and as a result the patient may complain of increased auditory acuity in the affected ear and of clicking noises.

Course.—Recovery is the rule, and in most cases during the second and third week the marked initial asymmetry of the face at rest diminishes as the still paralysed muscles regain tone. Voluntary movement appears first in the frontalis, then in orbicularis oculi, and last of all in the muscles round the mouth and in the platysma. Most cases begin to show voluntary movement within the first three or four weeks and then proceed to complete

recovery within about three months. In some instances, however, no visible movement is seen for at least four months, and in these circumstances full recovery may not be achieved and the restoration of movement may take over a year to reach its final stage. It is in these cases that during the third week the reaction of degeneration is found in the paralysed muscles. If at this period the muscles still respond to faradism an early and complete recovery may be expected. In elderly persons full recovery is less common than in young adults, and in them and in all slowly recovering cases some contracture of the weak muscles may gradually develop. This tends to minimize asymmetry of the face at rest, but on movement it may be a handicap, for each time the patient chews, the eye screws up and the lids almost meet. In these imperfectly recovered cases isolated movement of the upper or lower part of the face is not regained and the facial muscles contract as a whole.

Sometimes the lower lid sags permanently and tears trickle down the cheek.

So-called Geniculate Herpes.—Recent observations have rendered the status of geniculate herpes doubtful, and the facial palsy that sometimes occurs with herpes occipito-collaris may be a motor neuritis of the facial nerve comparable with that of the third nerve in some cases of ophthalmic herpes. Nevertheless the clinical picture of facial palsy with herpes deserves description. In a typical case the onset of facial paralysis is preceded by severe neuralgic pain in the external auditory meatus and pinna. There may also be similar pain in the fauces on the affected side and in the tongue. An eruption of herpetic vesicles then appears in the meatus on the adjacent parts of the pinna, sometimes behind the ear, on the pillar of the fauces, and on the anterior two-thirds of the tongue. The pinna may swell considerably and redden, the fauces show several ulcers when the vesicles burst, and look red and swollen. To the observer unfamiliar with this picture it is easy to make a diagnosis of septic throat with secondary infection of the middle ear, and the serous discharge from the burst vesicles in the meatus may be taken for an otorrhœa. When, as a climax, a facial palsy suddenly develops, the idea that the middle ear has been infected obtains an illusory confirmation. Not every case is so striking. Only a few vesicles may be seen in the meatus with no œdema of the pinna and no vesicles within the mouth. In these circumstances it is the facial palsy that first brings the patient under notice.

Bilateral Bell's palsy is not so uncommon as is generally supposed. When it occurs an interval of four or five days separates the involvement of the two nerves, and the bilateral paralysis of orbicularis oris leads to some difficulty in the formation of labials, so that articulation is not quite normal. *Recurrent* Bell's palsy may also occur, and in the course of a series of attacks both sides of the face may be involved. Occasionally, also, sixth nerve palsies may occur in the course of such a sequence.

Treatment.—In the majority of instances facial palsy makes a complete recovery within three months. For these cases it cannot be said that any treatment is essential or that the lack of it will prevent a favourable result. The residue of cases which over a period of from one to two years make a degree of recovery short of complete is composed mostly of elderly subjects, and requires more active measures.

In the third week after the onset, if no trace of return can be detected, it may be expedient to have the electrical reactions of the paralysed muscles taken. If they respond to faradism an early recovery can be expected. If

there be no response to faradism and if the response to galvanism is characteristic of the R.D., it is probable that no voluntary contraction will appear for three or four months and that thereafter improvement will be slow.

With these considerations in mind, and remembering that a Bell's palsy is a disquieting and disfiguring condition for the patient, some treatment becomes a psychological necessity from the outset. For the first week it is wise to keep the patient indoors and away from exposure to cold. The patient, a relative, or—if circumstances make it expedient—a masseur or masseuse should be instructed to rub the face gently with the finger-tips—moistened with ordinary olive oil—for about five minutes morning and evening, paying special attention to the muscles round the eye and the mouth. When, later, the patient begins to go outdoors the face is felt to be uncomfortably stiff after exposure to wind and cold. This discomfort may be relieved by bathing the face with a sponge wrung out of warm water for a few moments. No other measures than these are necessary. When recovery sets in they can usually be dispensed with. In the long-lasting cases where no tone returns to the paralysed muscles after two or three weeks and no voluntary movement in frontalis can be seen, it is wise to use a splint. This consists in a length of silver wire, one end of which is curved over the pinna like the sidepiece of a pair of metal spectacles, while the other—covered by a fine piece of rubber tubing—is bent and curved round the corner of the lip. When this is correctly adjusted, movements of the normal half of the face can no longer pull the lips across the midline and thus stretch the paralysed muscles.

This splint need not be worn during sleep.

Gentle massage of the kind already mentioned, which can perfectly well be performed by an amateur, should be continued. In no case of Bell's palsy can it be said that electrical stimulation of the paralysed muscles by galvanism serves any useful purpose. Indeed, if persisted in it may lead to disfiguring contracture of the partly recovered muscles. In brief, the hazard to which the subject of a Bell's palsy is exposed is that of excessive and ill-advised treatment rather than that of neglect.

Facial Spasm.—This is a malady of elderly persons, of unknown ætiology. The facial muscles go into momentary contraction in the form of an irregular clonic spasm. There may be a slight degree of maintained tonic spasm underlying this. It is always increased by emotion or by voluntary facial movements. As a rule it persists indefinitely and responds badly to all forms of treatment. In the most severe cases alleviation has been given by alcohol injections into the facial nerve, thus replacing spasm by paralysis which may be temporary, or more or less permanent. Clonic facial spasm may also be produced by compressing lesions of the nerve, or occur as part or all of a Jacksonian fit.

The Eighth Nerve

This nerve comprises sensory and non-sensory components. The sensory component is the cochlear nerve which subserves the auditory function. The non-sensory component is the vestibular nerve which subserves various reflex reactions concerned in the co-ordination of movement and posture. The two components are distinct peripherally and have separate central connections.

The nerves may be involved in their central course by focal lesions of the brain stem, in their intracranial course by tumours of the cerebello-pontine angle, or by gummatous meningitis in this region. The cochlear and vestibular

end-organs may be involved by suppurative processes in the petrous part of the temporal bone.

Symptomatology of the Cochlear Nerve.—Lesions of this nerve produce either deafness or tinnitus, or both combined. Slowly progressive pathological processes are prone to produce slowly developing deafness associated with tinnitus, as may be seen in the case of eighth nerve tumours, but these two symptoms are seen in a variety of conditions within the petrous bone itself in which the nervous elements are secondarily involved. Deafness due to a lesion of the nerve (nerve deafness) may be differentiated from middle ear deafness by the following tests : *The Weber test*—the foot of a vibrating tuning fork is placed upon the forehead. With nerve deafness the sound is best heard on the normal side while in middle ear deafness it is best heard on the affected side. *The Rinné test*—normally a vibrating fork is best heard when held slightly away from the ear. If it be placed upon the mastoid until it be no longer heard and then approached to the meatus it is heard again—in short, air conduction is better than bone conduction. In middle ear disease this relationship is reversed, and bone conduction is better than air conduction. In cochlear lesions both air and bone conductions are proportionately reduced. It may be added that the accurate differentiation of nerve from middle ear deafness may be a matter of considerable difficulty even in experienced hands.

Tinnitus is an extremely common symptom and may be due to local lesions in the external auditory meatus, in the middle ear, in the cochlear apparatus, or in the cochlear nerve within the skull. Occurring as an independent symptom it is commonly due to disease of the cochlea, when it is associated with slowly progressive deafness. It may occur in elderly subjects presenting signs of arterial degeneration, and may prove a distressing and intractable symptom. The noises are described as whistling, roaring, buzzing noises, or as like the sound of rushing or falling water.

Diagnosis.—The recognition of tinnitus presents no difficulty, and its cause must be determined by a systematic examination of the nervous system generally and of the auditory apparatus. When due to intracranial lesions, diagnosis depends upon associated signs of nervous involvement.

Treatment.—Occurring as an independent symptom it is generally intractable, but its intensity may be relieved by the administration of potassium iodide, the bromides, hydrobromic acid, or luminal.

Symptomatology of the Vestibular Nerve.—The labyrinth has two components, the semicircular canals and the otolith organs (utricle and saccule). The former are stimulated by movement, the latter by changes in the position of the head. The symptomatology of labyrinthine disease has not been fully elucidated in man, and the majority of symptoms attributable to this organ arise from disease of the semicircular canals. Vertigo is the most striking and best recognised symptom.

Vertigo.—True vertigo is a subjective sense of rotation, either of self or of surrounding objects. In intense vertigo consciousness may be disturbed or lost.

Vertigo may occur as a symptom in cerebellar disease, in lesions of the vestibular nerve and of the labyrinth, and also in cardiovascular disease, and in association with nausea and vomiting. In all these conditions the symptoms and signs of the underlying condition are to be found. Almost all cases of vertigo occurring in the absence of signs of disease elsewhere are due to chronic degenerative changes in nerve endings in the labyrinth. The

functions of the semicircular canals may be investigated by studying the nystagmus resulting from rotation of the patient, or from irrigation of the external auditory meatus with hot and cold water. These tests are highly complicated and require skilled employment.

Menière's Syndrome.—*Ætiology.*—This is a malady of adults, usually making its appearance in middle life, with a slight preponderance of male subjects. It is not associated with suppurative processes in the ear, nor with oro-nasal sepsis. The essential lesion appears to be a specific form of degeneration of the labyrinth characterised by distension of the endolymph system. There is also some measure of cochlear involvement, and although the associated deafness and tinnitus may seem to be restricted to one ear, there is usually a slight affection of the opposite ear.

Symptomatology.—The malady is characterised by sudden accesses of intense vertigo, with slighter interparoxysmal vertigo. These attacks occur at varying intervals of a few days or of a few weeks. They may be precipitated by sudden movements, by sneezing or blowing the nose, and there are reasons for supposing that reflexes arising in the nose may precipitate an attack. The sense of rotation may be purely subjective, or there may be an actual tendency to turn before falling. The subjective symptom may be of rotation of self or of surrounding objects, or of both. So intense is the giddiness that the subject usually falls down, sometimes with alarming suddenness. Consciousness may be momentarily lost. If the vertigo persists there is nausea and vomiting, the patient is pale and perspires profusely. The attack tends to pass off gradually, the symptoms being aggravated by any movement of the patient's head. Nystagmus and, rarely, diplopia may occur during the height of the attack. Associated inner ear deafness and tinnitus are present in many cases, if not at the onset of the malady then later during its course.

Course and Prognosis.—In most cases the early attacks are the most severe, and the disease tends slowly to improvement. In other cases there is progressive deafness, and when this is complete in the affected ear the vertiginous attacks cease. Under treatment some degree of alleviation occurs in most cases.

Diagnosis.—The occurrence of acute attacks of intense vertigo, especially when there are associated slight unilateral deafness with tinnitus and no signs of organic nervous disease, is characteristic of Menière's syndrome. In epilepsy, persistent deafness and tinnitus are absent, while in apoplectic seizures some objective signs of nervous lesion will be found, and vertigo is absent or transient and slight.

Treatment.—Phenobarbitone ($\frac{1}{2}$ gr. t.d.s.) and bromides usually have some beneficial effect in reducing the frequency and severity of attacks, but rarely give complete relief. Unilateral labyrinthectomy in severe and intractable cases, or incision of the saccus endolymphaticus, are more effective.

The Ninth, Tenth, and Eleventh Nerves

These nerves are so intimately related in their central connections, and are so frequently affected simultaneously in their contiguous peripheral course, that they are best considered together as the glossopharyngeal-vagus-accessorius complex. They contain both motor and sensory fibres. The motor fibres fall into two groups : (i) *a somato-motor* group which innervates the musculature of the pharynx, larynx, palate, sternomastoid, and trapezius.

The cells of origin lie in the nucleus ambiguus and its caudal extension. The latter reaches as far as the third cervical segment, where it forms the spinal nucleus of the accessory nerve. The musculature is represented in this columnar nuclear mass from before backwards in the order named above ; (ii) *a viscero-motor group* which supplies the involuntary musculature of the alimentary tract and of the air passages, and which arises in the dorsal nucleus of the vagus. The sensory fibres also fall into two groups : *a somato-sensory group*, the fibres of which end centrally in the substantia gelatinosa Rolandi and peripherally supply common sensation to the ear, mouth, pharynx, and the upper part of the respiratory tract ; and a larger *viscero-sensory group* which receives afferent fibres from the thoracic and abdominal viscera.

The three nerve trunks leave the skull together by the jugular foramen. The glossopharyngeal nerve ends in the posterior third of the tongue, the vagus extends downwards through the neck and thorax to the abdomen, while the spinal accessory (bulbar and spinal portions) sends its bulbar fibres to join the vagus, and its spinal fibres pass to the sternomastoid and trapezius muscles. These three nerves may be involved in focal medullary lesions and by lesions at the base of the skull or in the neck. Various symptom-complexes have been described corresponding to lesions in these different situations.

Lesions in the Medulla Oblongata.—These are not uncommon, and may be the result of focal thrombosis, chronic bulbar palsy, or of syringomyelia with bulbar extension. The symptoms (*syndrome of Avellis*) are unilateral paralysis of the soft palate, pharyngeal muscles, and larynx with an associated crossed hemianæsthesia of syringomyelic type affecting pain and thermal sensibility.

Paralysis of the soft palate is also a common symptom in diphtheritic paralysis, and is due to a lesion of the nucleus in the medulla.

Lesions at the Base of the Skull, either of the nature of new growth, fractures, or gunshot wounds, often produce associated ninth, tenth, and eleventh nerve palsies. The following syndromes have been described. *Schmidt's syndrome* : unilateral paralysis of pharynx, larynx, palate, sternomastoid, and trapezius. *Jackson's syndrome* : like Schmidt's syndrome, with the addition of a hypoglossal nerve palsy, but in incomplete forms the vocal cord may remain intact.

Lesions in the Neck.—*Tapia's syndrome* occurs in injuries high in the neck, and consists in unilateral paralysis of tongue and vocal cord (vocal fold), the palate being intact. The lesion is below the offset of the pharyngeal branches.

The characteristic sign of involvement of the glossopharyngeal nerve is sensory loss over the upper part of the pharynx and loss of taste in the posterior third of the tongue.

The characteristic signs of lesions of the vagus nerve are pharyngeal and laryngeal paralysis. In pharyngeal paralysis the soft palate lies low on the affected side and does not rise on phonation, and there is loss of the pharyngeal reflex on that side. Also, there is the so-called curtain movement of the posterior pharyngeal wall, which moves across to the normal side on swallowing. Bilateral pharyngeal paralysis may occur in diphtheritic paralysis.

Total unilateral laryngeal paralysis results from high level lesions of the vagus. The affected vocal cord (vocal fold) lies in the cadaveric position. There is weakening of the voice but no stridor.

Recurrent laryngeal nerve lesions, or lesions of the vagus below the offset of the superior laryngeal branches, produce paralysis of the abductor of the vocal cords. The affected vocal cord lies up against the median plane and does not move on phonation or on respiration. In bilateral abductor paralysis both vocal cords lie approximated in the midline and do not recede during inspiration. There is marked inspiratory stridor and considerable danger of asphyxiation (*vide* p.644, Tabes Dorsalis).

Lesions of the Spinal Accessory Nerve.—The bulbar portion joins the vagus at the ganglion of the trunk (inferior ganglion of vagus), and probably provides the majority of the motor fibres which reach the larynx through the vagus. It does not therefore need separate consideration. Lesions of the spinal portion produce sternomastoid and trapezius paralysis. It is paralysis of the latter which causes definite disability. The shoulder on the affected side cannot be raised fully. The scapula tends to fall away from the midline and to rotate so that its superior angle lies higher than normal, and protrudes as a hump on the contour of the neck as seen from in front. There is also some winging of the scapula, like that seen in serratus palsy, but most marked when the arm is held extended forwards below the horizontal, whereas the winging of serratus magnus (S. anterior) paralysis is maximal with the arm above the horizontal.

Ætiology of Glossopharyngeal-Vagus-Accessorius Lesions.—In the medulla, chronic bulbar palsy, focal thrombosis, tumours, syringobulbia, and diphtheritic toxic lesions may all produce symptoms referable to one or more of these nerves. In their intracranial course, tumours or syphilitic meningitis may involve one or more of them. At the base of the skull, injuries or new growth may involve all three in the region of the jugular foramen, while in the neck, injuries, new growths, or aneurysms may compress them. The vagus may be involved in the thorax (recurrent laryngeal paralysis) by aneurysm.

Glossopharyngeal Neuralgia.—This comparatively rare condition is in the characteristics of the pain very like trigeminal neuralgia. The patient complains of accesses of severe neuralgic pain in the region of the throat and ear. The paroxysm is commonly excited by the act of swallowing. The patient is usually a middle-aged or elderly man.

Treatment resembles that of trigeminal neuralgia in the matter of medication. In severe and intractable cases division of the glossopharyngeal nerve within the skull has been successfully performed.

The Hypoglossal Nerve

The twelfth nerve is an exclusively motor nerve which arises in a group of cells on the floor of the fourth ventricle close to the median plane. Its fibres innervate the muscles of the tongue and some of the elevators of the hyoid bone (hyoglossus and genio-hyoid).

Ætiology of Lesions.—The nerve nucleus may be involved in medullary lesions, particularly in chronic bulbar paralysis, syringobulbia, tumour, thrombosis, and sometimes in tabes dorsalis. The two nuclei lying close together are generally both affected. The nerve may be affected in its intracranial course by syphilitic meningitis or new growth. Peripherally, it may be involved alone, or, as we have seen with vagus and accessorius, in any disease process deep in the neck.

Symptomatology.—Lesions of the cortico-bulbar (upper motor) neurones at any level higher than the pons may affect the tongue, rendering the organ spastic and small and causing protrusion towards the side of the lesion.

Nuclear or infranuclear lesions lead to unilateral paralysis, the organ when protruded being thrust towards the paralysed side by the unopposed muscles of the normal half; wasting and fibrillation also occur. The organ on the affected side is shrunken and wrinkled and is in constant fibrillation.

COMPRESSION OF THE SPINAL CORD

The spinal cord may be subjected to gradual compression or may be suddenly crushed. The symptom-complex of sudden and complete compression is that of anatomical transection of the cord, and will be described under the heading of Total Transverse Lesions of the Cord (*vide* p. 678).

Gradual compression, apart from injury to the spine, is the common form of compression, and may be due to a variety of causes.

Gradual Compression

Ætiology.—The cord may be gradually compressed by disease of the vertebral column, of the meninges, or of the nerve roots. Further, tumours developing in the substance of the cord also effect compression as they increase in size.

The form of vertebral disease responsible for most cases of compression paraplegia is tuberculous caries. This is commonly situated at some level between the fourth and tenth thoracic vertebræ, and may compress the cord in one of two ways. A tuberculous abscess forming in the vertebral body may bulge backwards into the vertebral canal on either side of the posterior common ligament, or tuberculous granulation tissue may invade the canal and, directly involving the theca, produce a localised meningitis with resulting constriction of the cord. It is important to remember that cord compression can occur in the absence of visible deformity (angular curvature) of the spine. Children and young adults form the majority of patients so affected.

Osteomyelitis and, more commonly, malignant disease of the vertebræ may cause cord compression. The latter is especially common after excision of the breast for carcinoma. In this case it is the lumbar cord that generally suffers and the clinical picture is a very characteristic one. Primary sarcoma and hypernephroma may also invade the vertebræ and lead to compression of the cord. Finally, erosion of the vertebral column by aortic aneurysm may produce a like result.

The meningeal diseases which may lead to cord compression are syphilitic pachymeningitis, particularly in the cervical region, localised meningitis from vertebral osteomyelitis, and meningeal tumours.

Similar in nature to meningeal tumours, which are mainly intrathecal, are the benign fibromata which sometimes develop on the spinal nerve roots and lead to compression of the cord.

Occasionally, vertebral injury may be associated with rupture and herniation of an intervertebral disc, the herniated portion then becoming a compressing lesion of cord or of nerve roots. This may occur in the cervical, thoracic, or lumbar regions.

Morbid Anatomy.—The cord may be compressed to a ribbon-like structure at the level of compression, or in the case of a tumour arising on a nerve root, the neoplasm may be found to have made for itself a pocket on one side of the cord. Microscopically there may be necrosis of both grey and white matter in the compressed segments, and at its upper and lower limits neuroglial reaction and phagocytic activity are seen, together with venous engorgement. Ascending tracts are found to be degenerated above and descending tracts below the level of the lesion. This descending degeneration, even in long-standing cases of compression, may be very incomplete.

The Cerebrospinal Fluid (*Froin's Compression Syndrome*).—The compressing lesion may obliterate the subarachnoid space. When this happens the cerebrospinal fluid in the distal portion of the space stagnates and undergoes changes in composition and appearance, approximating more closely to blood plasma in the former respect. The total protein content may rise to many times its normal amount—for example, 0·5 or 1·0 per cent. The fluid may also assume a yellowish tinge (xanthochromia). If the compressing lesion be inflammatory in nature (meningitis) there may also be an increase in the cell content of the fluid, the cells present being mononuclears. In slighter degrees of alteration an increase in the protein content may be the only definite abnormality.

Symptomatology.—There are minor variations in the clinical picture of spinal cord compression according to the nature of the compressing lesion, but in general the sequence of events is remarkably constant. The symptoms are of two orders: (i) those arising at the level of compression, and (ii) those due to interference with the long ascending and descending tracts of the cord. Of the former, the symptoms due to compression of spinal nerve roots are of great diagnostic importance.

At the level of the lesion, both anterior and posterior roots are commonly compressed. The posterior root symptoms are the more constant and prominent. They consist of sharp pains radiating along the course of the root and referred to its distribution. They may be periodic or almost constant. When thoracic roots are bilaterally affected, the pains encircle the trunk and are known as "girdle pains." When a single root is affected on one side the pain is confined to one-half of the body. In the case of the roots which enter into the limb plexuses, the pains are referred to the corresponding limb down which they spread. The pain may be accompanied by hyperæsthesia and sensory impairment. Root pains may be the first indication of disease, and may precede all objective signs of root or cord compression by weeks or months. Secondary carcinoma of the spine is frequently ushered in by sudden root pains on exertion, and the occurrence of sudden girdle or back pains in an individual known to have had visceral or mammary carcinoma is of sinister significance.

In the case of fibroma on a spinal nerve root, more or less constant pain in a nerve root distribution may be present for long periods before signs of cord compression appear. On the other hand, all such symptoms may be absent in a given case of spinal cord compression. Symptoms referable to ventral roots are not so common, and in the case of the roots which lie between the upper and lower limb plexuses may escape notice. In the case of the cervical and lumbo-sacral roots, however, wasting and fibrillation of corresponding limb muscles is not uncommon. Rarely, irregularly clonic muscular spasm may be present.

The diagnostic importance of root symptoms lies in the fact that they give information as to the level of compression.

The gradual compression of the cord itself leads to progressive interference with conduction in the long spinal tracts, both ascending and descending. Usually motor symptoms appear before sensory changes, and there is often a period in the early evolution of a case of compression when the absence of sensory loss may make segmental localisation impossible. The motor disturbance consists in the gradual development of spastic weakness, with increase of tendon jerks, the appearance of clonus and of the extensor or Babinski type of plantar response. Probably the earliest objective signs are the extensor plantar response, increased tendon jerks, and weakness of dorsiflexion of foot and toes.

As compression becomes more severe, the legs become progressively weaker and the condition of *paraplegia in extension* develops.

The extensor and plantarflexor groups of muscles in the legs are extremely spastic and go periodically into clonus, in which the whole limb is shaken. The voluntary power of flexion and dorsiflexion wanes far in advance of that of extension and plantarflexion, and the patient, while still able to stand and walk, does so with stiffly held legs and shuffling feet.

Finally, powerful spontaneous flexor spasms make their appearance, all voluntary power disappears, and the limbs come to lie in a position of full flexion, with the knees pressed against the abdominal wall. This is the condition of *paraplegia in flexion*. The knee and ankle jerks may disappear, but stimulation of the sole produces a brisk extensor plantar response with powerful flexion at hip and knee, which is sometimes bilateral.

Soon after the development of early signs of spastic weakness, loss of sensation involving all forms of sensibility makes its appearance and gradually extends up to the level of the distribution of the posterior root fibres of the segment immediately below the level of compression. Separating the region of sensory impairment from the higher levels of normal sensation, there may be a zone of hyperæsthesia in the distribution of the compressed roots, but this is not a constant finding.

The abdominal reflexes are also abolished early below the level of compression. In the case of compression of the tenth thoracic spinal segment, for example, we should find spastic paresis of the lower limbs, weakness of the abdominal muscles below the level of the umbilicus, with deviation upwards of the umbilicus on contracting the abdominal wall (Beevor's sign), loss of the abdominal reflexes below the umbilicus, and sensory loss below the same level. Thus motor, reflex, and sensory phenomena all contribute to establish the segmental level of compression.

Generally a little later than the establishment of motor and sensory symptoms, disturbances of sphincter control appear. At first, precipitancy of micturition and then periodical evacuation of urine occur, but the bladder is never completely emptied. There is always residual urine after this so-called reflex micturition, and the term "overflow incontinence" is a more accurate one to use in this connection.

With compression of fairly rapid onset, retention of urine may be the initial sphincter symptom. In respect of the bowel, constipation and fæcal incontinence after purgatives are the usual symptoms.

By the time that paraplegia in flexion has developed, voluntary power, sensation, and sphincter control are almost if not completely lost below the

level of the lesion. Bedsores over the sacrum and trochanters develop, and septic absorption from this source and from cystitis hasten a fatal issue.

In the case of spinal caries, the symptoms are commonly of equal intensity on both sides, and the cord sustains a generalised compression. With spinal nerve root tumours, on the other hand, the lateral position of the compressing lesion often leads to wholly or predominantly unilateral signs. A *Brown-Séquard syndrome* may develop in these circumstances. The anatomy of the spinal cord and the course of afferent and efferent paths will indicate what this syndrome must be. On the side of the lesion there is spastic weakness of the corresponding leg, with the appropriate alterations in the reflexes. There is also loss of the sense of position and of vibration sense in the paretic limb, with some sensory ataxy. Tactile, thermal, and painful sensibility are intact. On the side opposite to the lesion, motor functions are intact, as are the sense of position and vibration sense, but there is loss or impairment of tactile, painful, and thermal sensibility. At the level of the lesion and on the same side there may be a zone of hyperæsthesia or of sensory impairment to all forms of sensation corresponding to the root actually compressed.

Further, certain physical signs are peculiar to particular segmental levels of the cord, and are of importance in *segmental localisation of the lesion.*

Motor Localisation.—The list of muscles with their segmental innervation given in the table below indicates the muscles in which wasting and other signs of a lower motor lesion must be looked for at different segmental levels of compression.

Segmental Representation of Muscles

C. 4.	Scaleni, trapezius, levator anguli scapulæ, diaphragm.
C. 5.	Levator anguli scapulæ, scaleni, supraspinatus, rhomboids, infraspinatus, teres minor, biceps, brachialis anticus, deltoid, supinator longus (brachio-radialis), serratus magnus (s. anterior), pectoralis major (clavicular part).
C. 6.	Subscapularis, pronators, teres major, latissimus dorsi, serratus magnus, pectoralis major.
C. 7.	Triceps, extensors of wrist and digits.
C. 8.	Flexors of wrist and digits, small hand muscles.
Th. 1.	Interossei and small hand muscles.
Th. 2 to 12.	Intercostals, abdominal muscles.
L. 1.	Quadratus lumborum.
L. 3.	Sartorius, adductors of hip, ilio-psoas.
L. 4.	Quadriceps extensor femoris, abductors of hip.
L. 5.	Flexors of knee.
S. 1.	Calf muscles.
S. 2.	Glutei, peronei, anterior tibial muscles, small foot muscles.
S. 3, 4.	Pelvic muscles.

Sensory Localisation.—Fig. 28 provides corresponding information for determining the segmental level from the sensory loss.

Reflex Localisation.—Tendon reflexes, the reflex centres of which lie in the compressed segment or segments, may be abolished or changed. The segmental representation of the main tendon reflexes is as follows : biceps jerk, fifth cervical segment ; supinator (brachio-radialis) jerk, fifth and sixth cervical segment ; triceps jerk, sixth and seventh cervical segment ; knee jerk, fourth lumbar segment ; ankle jerk, first sacral segment.

Lesions involving the grey matter of the fifth cervical segment may produce what is known as inversion of the supinator jerk. This jerk is replaced by finger flexion. This sign is not infrequently seen in syringomyelia, traumatic lesions of the cord due to dislocations or fractures of the cervical spine, and in spinal tumours at the fifth cervical level. Similarly, in lesions

involving the first sacral segment. a hamstring jerk only may occur on tapping the tendo Achillis.

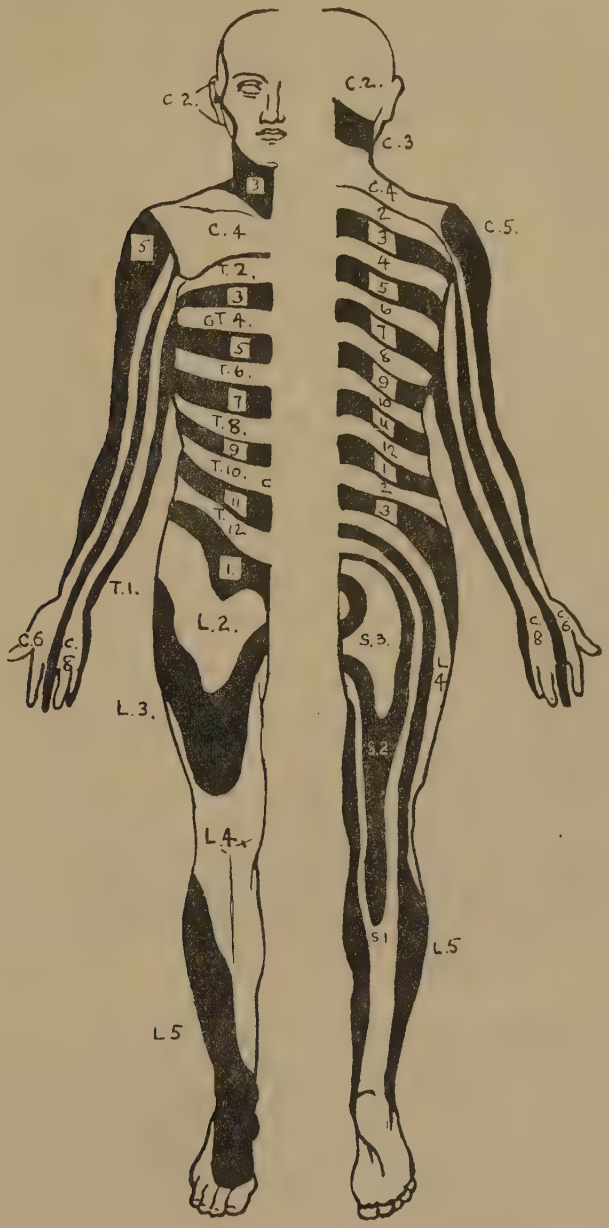

FIG. 28

The cutaneous areas supplied by the posterior nerve roots.

The Cervical Sympathetic.—The signs of paralysis of the cervical sympathetic may be associated with lesions involving the lowest cervical and first thoracic segments or their spinal nerve roots. These are pupillary

myosis, enophthalmos, and a narrowing of the palpebral fissure, also lesions of the cervical cord, if they interfere with the bulbo-spinal sympathetic fibres, will produce this symptom-complex (Horner's syndrome).

Temperature disturbances are occasionally associated with cervical cord lesions. Of these hyperpyrexia is the commoner, but abnormally low temperatures (86° to 90° F.) are very rarely seen.

Conus Medullaris and Cauda Equina.—The cauda equina includes all the spinal nerve roots below the second lumbar roots, and hence the motor and sensory symptoms resulting from compression of this structure will depend upon the particular roots involved. The motor symptoms will be of lower motor neurone type, that is, flaccid paralysis with atrophy. The knee and ankle jerks may be abolished. Sensory loss will be restricted to the area supplied by the lower four lumbar and all the sacral dorsal roots. Frequently only the sacral roots are compressed. There may be loss of the ankle jerk and sensory loss over the sacral root areas, *i.e.*, the perineum and posterior aspect of the leg with the sole of the foot. Fractional parts of this motor and sensory symptomatology occur when a smaller number of roots are involved. The sphincter disturbances corresponding to these various lesions consist in overflow incontinence of urine with incontinence of fæces.

In the case of the conus medullaris, the motor symptoms are very like those resulting from lesions involving the cauda equina, in being of lower motor neurone type and of comparable distribution. The sensory loss also is much the same, but there may occasionally be dissociated anæsthesia. The great pain of root distribution, which may attend lesions of the cauda equina, is commonly absent in conus lesions.

We may appropriately refer here to the clinical picture characteristic of secondary carcinoma of the spine. There may be multiple deposits in the vertebræ, but the lumbar spine tends to be early and severely involved. The sequence of events is commonly as follows : Some two or more years after the excision of a carcinoma of the breast the patient, while making some physical effort, experiences sudden intense pain in the back. These " alarm pains " as they have been called, recur at increasingly short intervals and may be present for some months before examination reveals any local or neurological signs. Finally, the signs of compression of the lumbar enlargement and lower end of the cord make their appearance. Death usually intervenes, from the presence of malignant disease elsewhere in the body, before paralysis becomes profound.

Diagnosis of Gradual Compression.—The differential diagnosis of slowly developing spastic paraplegia may be attended with considerable difficulty. In the case of vertebral disease, the development of a localised tenderness or of local pain, or again of deformity, will reveal the situation and nature of the lesion. But both in malignant disease and in spinal caries, root and cord compression may appear before deformity. In this case radiography may reveal what clinical examination of the spine fails to show. Rigidity of the spine is common in vertebral disease, but may also occur in the case of meningeal or nerve root tumours. In the case of compression from disease (tumours, meningitis) within the vertebral canal, the presence of a great excess of protein in the cerebrospinal fluid (Froin's syndrome) may confirm the presence of a local block in the subarachnoid space. The persistence of root pains, though not a constant phenomenon, is often of great diagnostic and localising value. In meningeal and nerve root tumours the signs of root and cord compression

are commonly unilateral at onset but bilateral in vertebral disease. It is usually impossible to differentiate extra-medullary and intra-medullary spinal tumours.

The differentiation of compression from other focal or diffuse cord lesions may also be difficult. In the so-called spinal form of disseminated sclerosis, careful examination will usually reveal one or other of the following signs: slight nystagmus, pallor of one or both optic discs, or a pathological increase in the tendon jerks of the arms, while a careful case history will reveal the long past occurrence of transient blindness of one or both eyes, of diplopia, or of temporary ataxy of an arm. Further, cutaneous sensory loss is very exceptional in early disseminated sclerosis, the usual sensory change being a loss of vibration sense in the legs, with or without slight impairment of the sense of position in these limbs.

In a few cases of amyotrophic lateral sclerosis, signs of lateral sclerosis (spastic paresis of the legs without sensory or sphincter disturbance) may antedate the appearance of wasting in the hands. The patient is usually a middle-aged man, there is no history of root or other pains, and the arm and jaw jerks may be extremely brisk. Wasting of the intrinsic muscles of one or both hands commonly appears within a year of the onset of spastic weakness of the legs.

The presence of spastic weakness of the legs with sensory changes showing a more or less distinct and a constant upper level, with reflex changes strictly confined to the regions below this level, and the characteristic changes in the cerebrospinal fluid, are essential to a diagnosis of spinal compression, but some cases remain without one or other of these signs, and diagnosis cannot be certain without an exploratory laminectomy. An additional diagnostic method is now available in the intrathecal injection through the atlanto-occipital membrane of an opaque contrast medium such as pantopaque. This being opaque to the X-rays and heavy, tends to sink in the theca until it encounters a block, where its retention may be revealed by radiography. This method involves skilled procedure and should be reserved for those cases where it is absolutely essential for a differential or a localising diagnosis. An alternative procedure is to inject pantopaque by the lumbar route, the patient being on a tilting X-ray table. The opaque fluid then runs headwards to the lower limits of the obstructing lesion, where it may be radiographed.

Sudden Compression of the Cord

This is almost invariably the result of vertebral injuries, but may occasionally result from the sudden collapse of a vertebral column which is invaded by malignant disease. In the case of indirect violence the cervical spine is most commonly involved, fracture or fracture with dislocation occurring between axis and atlas, or between the fifth and sixth cervical vertebræ. Death commonly follows the first of these, but after the second every grade of spinal cord injury may be seen. Any violence which forcibly flexes the head on the neck, such as falls from horses or diving into shallow water, may produce fracture with dislocation between the fifth and sixth cervical vertebræ. It is important to remember that in such cases attention to the scalp wound may lead to a neglect to consider the possibility of vertebral injury.

The other situation in which the spine may be fractured is the

dorso-lumbar region. Falls from a height in which the individual drops standing on his feet, or strikes his back on some projecting object, usually involve this region and produce severe crushing of the cord.

Morbid Anatomy.—In severe compression the cord is pulped at the level of injury and the damaged tissue rapidly necroses and becomes diffluent. At the upper and lower limits of damage, œdema and serous effusion with slight hæmorrhage are found. Later, there is a glial reaction with active phagocytosis at these points. If the subject survive long enough, ascending and descending degenerations are to be seen.

In the less severe lesions sustained in most cases of fracture-dislocation of the lower cervical spine, the cord is only momentarily compressed or nipped, and may with the partial return of the vertebræ to the normal be freed from permanent compression.

Symptomatology.—Sudden compression, even when the cord is not completely crushed, frequently results in complete flaccid paraplegia with total sensory loss below the level of the lesion. There is also retention of urine and intense priapism. Bedsores develop with extreme rapidity over the sacrum. In high cervical lesions death may ensue from paralysis of the respiratory muscles, while with lower level lesions septic absorption from bedsores or from a bladder infected by catheterisation may also lead to a rapidly fatal issue.

When the structural damage is less severe, this stage of total interruption of conduction through the lesion is short and some return of power and of sensation occurs. In the case of the lower cervical spine, atrophy and paralysis of varying degree and extent is found in the arms (corresponding to damage to the grey matter of the crushed segments), with a varying degree of spastic paresis and sensory loss in the lower limbs. In some cases recovery is almost complete, but many patients are left with severe residual disability. The more severe grades of paralysis following injuries of the cervical spine are readily recognised, but the slighter grades may escape recognition. In these there is slight spastic paresis of the legs, with the appropriate changes in the reflexes, and some spasticity of the arms with wasting of the hand muscles. After the first few weeks, sensory loss may be minimal or absent and the condition is apt to be diagnosed as amyotrophic lateral sclerosis. A history of sudden onset following a fall or injury involving the head or neck, the persistence of pains in the neck, shoulders, or arms, limitation of movement of the neck, and inversion of the radial reflexes in the arms should make a correct diagnosis possible.

Total Transverse Lesions of the Cord.—It will be mentioned that sudden transverse lesions of the cord, either traumatic or inflammatory (*vide* "Myelitis," p. 683), may for the time produce a complete interruption of conduction through the damaged segments, apart from anatomical solution of continuity. The clinical picture of such interruption consists of total flaccid paralysis and sensory loss below the level of the lesion, total abolition of the tendon reflexes and of the abdominal reflexes, and retention of urine. In respect of the plantar responses, the initial finding varies. There may be no plantar response, there may be a plantar flexion movement of the great toe, or there may be a feeble Babinski type of response. The anal and bulbo-cavernosus reflexes are often preserved. The skin overlying the paralysed region is dry, and rapidly becomes shiny and tends to crack. Bedsores appear rapidly unless great care is taken to prevent their formation. There may be marked

œdema of the feet and ankles, which are cold. The isolated portion of the spinal cord, therefore, shows no reflex activity of any kind except in respect of the two reflexes mentioned as sometimes retained.

If, with the exercise of great care, infection of the bladder and the development of bedsores be prevented, this initial stage of *spinal shock* gives place in about the third week to a slowly developing phase of *spinal reflex activity*. The limbs remain paralysed and completely insensitive, but the flexion reflex, which was described in the introductory chapter to this section (*vide* p. 673), gradually emerges from shock. The receptive field of the reflex, that is, the area from which it can be elicited, spreads so as to include the whole sole, and gradually, during the course of weeks, spreads up the leg so as finally to include the skin of the whole limb and even the abdominal wall below the level of the lesion. Any stimulus within this extended region will evoke the appropriate reflex response. Further, stimulation of deep structures (tendons and muscles) also suffices to evoke the response. The response itself also progressively increases in extent and intensity. At first feeble dorsiflexion of the hallux and feeble contraction of the hamstrings alone occur ; later, flexion at ankle, knee, and hip are added, and finally, with complete restoration of reflex activity, almost any strong stimulus to the limb evokes a powerful flexion spasm, including dorsiflexion of ankle and toes. This response is often bilateral, and may be accompanied by powerful contraction of the abdominal muscles. Also, retention gives place to periodical evacuation of urine. But in both circumstances the bladder is not fully emptied, some residual urine being retained. The knee and ankle jerks may reappear.

With the passage of time the legs tend to go into the condition described earlier as that of paraplegia in flexion, and stimulation of the limb evokes, simultaneously, powerful bilateral flexion of the legs, the passage of urine, and an outburst of sweating over the paralysed parts of the body.

In the majority of cases the subject succumbs before the phase of spinal shock has been passed, and for the reasons which have been given. If he can be tided over this period, the tendency to the development of bedsores diminishes, the bladder does not require such frequent catheterisation and is not so readily infected, and life may be prolonged for years, but no restoration of motor or sensory function is possible.

Treatment.—The treatment of a case of compression paraplegia varies with the nature of the lesion responsible and sometimes with the acuteness and the completeness of the compression. In the case of spinal caries prolonged immobilisation in plaster or on a suitable frame is necessary. Benign spinal cord tumours are amenable to removal, but malignant disease of the spine causing compression can be treated symptomatically only. Relief of pain is sometimes obtained by the operation of cordotomy : that is, by bilateral division of the spinothalamic tract. Occasionally deep X-ray therapy relieves pain in vertebral malignant disease.

Sudden compression from injury, *e.g.*, gunshot wounds, fractures, or dislocations, varies from slight to severe cord damage. Decompressive laminectomy may be called for when there is evidence of narrowing of the vertebral canal, while in cervical injuries fixation of the neck in plaster may be necessary.

Retention of urine may be dealt with by suprapubic cystotomy, tidal drainage, or catheterisation, and in all cases infection of the urinary tract may require treatment. For this purpose the sulphonamides and penicillin

are available. The care of the back, trochanters, and heels is important to avoid the development of bedsores. The back, when the skin is intact, should be washed with soap and water four-hourly and rubbed with spirit. In complete transection of the cord, despite all possible precautions, a sacral bedsore commonly develops. If by prophylactic medication the bladder can be kept free of infection the formation of decubitus calculi may be averted.

SYRINGOMYELIA

Syringomyelia is a chronic progressive disease of the spinal cord, characterised by the presence of a cavity of varying length within the cord. The cavity arises in a rest of embryonic tissue in the region of the central canal. This undergoes proliferation during early life and breaks down at its centre with the formation of a cavity. The symptoms appear during early adult life, and are the result of compression of normal structures in the cord by the enlarging lesion.

Ætiology.—Both sexes are equally affected. There are said to be no hereditary or familial factors. Occasionally, however, symptoms may appear in childhood, and in some cases kypho-scoliosis developing at this period has been the first sign of the malady. It may be accompanied by the presence of other structural abnormalities of congenital origin, such as spina bifida, or deformities of the skull and bones. Hence the name " status dysraphicus " which has been applied to these conditions.

Morbid Anatomy.—The glial proliferation, or gliomatosis of syringomyelia, appears to originate in the neighbourhood of the grey commissure of the cord. On inspection the cervical, and less commonly the lumbar regions of the cord, may be irregularly enlarged, owing to the dimensions of the enclosed cavity at these levels. Serial sections through the cord reveal the presence of a central gelatinous mass of glial tissue enclosing a cavity, which varies in size from segment to segment and contains a fluid which may be clear and watery or glairy in consistence.

In some regions the cavity is large and its glial wall thin ; in others a dense glial mass contains a narrow cavity. The process may extend from end to end of the cord, and sometimes passes upwards into the medulla. Here it has the appearance of one or more fissures radiating ventrally and laterally from the floor of the fourth ventricle and contained by walls of glial tissue.

Degenerative changes in both grey and white matter are present, due in part to compression and in part to actual invasion and destruction of the nervous elements by the proliferating glial tissue.

The lower cervical and upper thoracic segments are almost always the region in which the nervous tissue is most severely damaged, and are therefore the regions to involvement of which most of the clinical manifestations of the disease are due.

Symptomatology.—The nature and topography of the symptoms may be deduced from the situation of the lesion that has been described above. They may be classified as under : (i) Sensory changes due to compression of the sensory fibres subserving thermal and painful sensation, as these fibres pass from the posterior horn across by the grey commissure to the lateral column of the opposite half of the cord ; these may be interrupted over a number of segments. (ii) Atrophic paralysis of lower motor neurone type of

a distribution corresponding to those segments in which the grey matter of the ventral horns is damaged. (iii) Spastic weakness of the lower limbs due to compression of the pyramidal tracts, as these traverse the severely compressed segments. (iv) Trophic and vasomotor symptoms.

Sensory Symptoms.—From what has been said above it is clear that there is commonly a "dissociated sensory loss" in syringomyelia. The forms of sensation which travel by crossed paths, namely, temperature and pain sensibility, are lost; those which travel by an uncrossed path in the posterior column, namely, the sense of active and passive movement and certain aspects of tactile sensibility, remain intact. This dissociation is not constant, and in some advanced cases all forms may be impaired. The topography of this peculiar sensory disturbance varies from case to case. The characteristic feature, however, is that there is both an upper and lower level of loss. The upper level may reach the limits of the cutaneous distribution of the fifth cervical nerve or some lower level, while inferiorly it may reach any of the thoracic segmental areas. It rarely extends below the thoracic region. It may be unilateral or bilateral, and when bilateral may be asymmetrical. Subjective sensory disturbances are relatively infrequent, and when present generally consist of pain referred to one or more of the segments in which there is sensory loss. A common result of the loss of pain sense in the hands is that the subject burns his fingers when holding hot objects, and is made aware of the burn only by the appearance of a blister. On the hands of such a patient the scars and recent ulcers of such injuries may be a conspicuous feature.

Muscular Atrophy.—Wasting is most frequently seen in the small hand and forearm muscles. It may, however, be found in other regions, such as the scapular region, and in the case of lumbo-sacral involvement, in the lower limb. Like the sensory loss, it may be unilateral or bilateral and asymmetrical, the latter condition being more common. The wasting tends to reach a certain degree of intensity, and there to be arrested short of total loss of muscle fibre. In some muscles, however, it may become complete. Deformities of the hand are common, with severe wasting, claw-hand being the usual type.

Spastic Paresis of the Legs.—This is not a constant or an early feature, and does not usually become severe.

Trophic and Vasomotor Symptoms.—Rarefaction of the bones of the upper limb and Charcot's osteoarthropathy in shoulder or elbow joints may be present. These lesions are particularly apt to occur in labouring men in whom the bones and joints are peculiarly exposed to strain. Extremely common is a condition of the hands in which they become red or cyanosed in colour and puffy in appearance and consistence, owing to a diffuse thickening of the subcutaneous tissues. This is the so-called succulent hand. This state of the tissues and the particular liability to injury dependent upon the analgesia, lead to the presence of infected wounds and ulcers, of whitlows and sometimes to necrosis of the terminal segments of the digits.

Cases with prominent deformities arising in this way were formerly spoken of as cases of Morvan's disease. It is characteristic of lesions of this kind that they are painless throughout their course.

Other symptoms sometimes met with are signs of paralysis of the cervical sympathetic (enophthalmos, myosis, narrowing of the palpebral fissure, and disturbance of sweat secretion over face and forequarter), when the last cervical and first thoracic segments are severely involved.

Syringobulbia.—The signs indicating spread of the lesion into the medulla are nystagmus (involvement of the posterior (medial) longitudinal bundle), hemiatrophy of the tongue (involvement of the hypoglossal nucleus), rarely facial paresis (involvement of the facial nucleus), unilateral paralysis or paresis of the palate, pharynx and larynx and sternomastoid (involvement of the vagus-accessorius nuclear complex), or analgesia of a peripheral zone of the face (involvement of the spinal root of the trigeminal nerve). Of all these, hemiatrophy of the tongue, sensory loss on the face, and nystagmus are the most frequently encountered.

Skeletal Deformities.—Kypho-scoliosis is practically a constant phenomenon in syringomyelia, and may reach an extreme degree of deformity. Other deformities are asymmetry of the skull and pes cavus, and occasionally spina bifida. A number of cases in which syringomyelia and acromegaly have been associated are on record.

Course.—The progress of the disease is usually very gradual, and may be completely or partially arrested for a long period of years at any stage. Rarely, hæmorrhage into the cavity or its sudden distension may lead to an acute increase in symptoms, and sometimes to severe paraplegia of the legs. Intense pain is apt to accompany these events. Death may ultimately ensue after many years from respiratory paralysis or from intercurrent affections.

Diagnosis.—In the early stages this may be rendered difficult by the fact that muscular atrophy may precede sensory loss; or conversely, sensory loss of dissociated type may appear before there is any wasting. In either case, the presence of spinal and other deformities is of diagnostic value. In respect of the motor symptoms, the combination of wasting of the forearm and hand muscles, with signs of spastic weakness of the legs, is common to both syringomyelia and amyotrophic lateral sclerosis. In the latter there is no sensory loss, the tendon jerks in the arms are exaggerated, there are no skeletal deformities, and the patient is commonly a middle-aged man. Intra-medullary or extra-medullary tumours of the cervical region of the cord may also produce a comparable motor picture. Here, also, skeletal deformity is absent, and there is sensory change, not dissociated in type and involving all the body below the level of the lesion. Progressive paraplegia with sphincter disturbance and root pains of constant distribution, and the absence of trophic and vasomotor symptoms, all serve to distinguish compression by meningeal or nerve root tumour or by pachymeningitis from syringomyelia.

Cervical rib, when it is manifested by the development of wasting of the muscles of one hand and by pain in the arm, may be mistaken for an early manifestation of syringomyelia. In the former, the signs remain unilateral and confined to the arm, there is little or no sensory loss of any kind, and the wasting is selective in incidence, in many cases being confined to opponens and abductor pollicis.

Treatment.—In general, we may say that the malady is uninfluenced by any form of treatment and slowly progresses unchecked. X-ray therapy to the region of the cervical spine has been extensively employed but with uncertain results. It may relieve pain in those cases where this is a distressing feature.

HÆMATOMYELIA

True hæmatomyelia is an exceedingly rare condition. Commonly said to be traumatic in origin, the fact is that crushing injuries of the spinal cord

produce softening but not massive hæmorrhage. Such hæmorrhage when it occurs is associated with abnormalities in the spinal vessels or with other forms of arterial disease; *e.g.*, in syphilis. The symptoms consist in a sudden development of a paraplegia, usually cervical in level, with severe pain. Thereafter a more or less incomplete recovery process sets in.

ACUTE AND SUBACUTE NECROTIC MYELITIS AND MYELOMALACIA

Under these titles we deal with cases of paraplegia of acute or subacute origin that become complete and flaccid and usually end fatally.

Ætiology.—As the titles imply, the pathogenesis of these rare cases is obscure. The acute cases have in the past been called "acute infective myelitis," but nothing is known of their bacteriology. Some of them appear to result from thrombosis of spinal arteries and others from a primary obliterative sclerosis of small intra-medullary and meningeal vessels in the lower segments of the cord. The degeneration of the cord appears secondary to the vascular lesions. To express the current view that they are toxi-infective in origin is to reveal how little we know of their causation.

Morbid Anatomy.—In the so-called necrotic cases the areas of spinal cord necrosis are associated with a small obliterated artery, and sometimes with thickening of the larger veins. The necrosis affects the grey matter more severely than the white. In frank spinal arterial thrombosis the affected segment or segments of the cord become soft and diffluent, and all signs of normal structure are lost. The cerebrospinal fluid usually shows a small increase of cells (lymphocytes) and of protein.

Symptomatology.—The onset may be febrile or afebrile. In the acute cases paraplegia develops rapidly and becomes complete (syndrome of total transection) within a day or two. In the subacute cases this state is reached within two or three weeks. The paralysis may ascend after its initial appearance. The patient may succumb early, or may survive with profound paraplegia, sensory loss, and sphincter paralysis. In the latter case a final stage of paraplegia in flexion, or of paraplegia in extension, may be reached.

Diagnosis.—The possibility of syphilitic meningo-myelitis, which is more frequently seen, has to be considered, and when this is present the cerebrospinal fluid will show an increased cellular and protein content, a positive Wassermann reaction and the colloidal gold reaction described on page 636. In elderly persons, spinal thrombosis may be responsible for a sudden complete paraplegia. In this case the cerebrospinal fluid remains normal.

Treatment.—The lesion is established so rapidly that little but symptomatic measures can be carried out. It is of the utmost importance to protect the bladder from infection should catheterisation be necessary, and to prevent the development of bedsores. Therapeutic lumbar puncture may conceivably be of value, and the administration of massive doses of hexamine may be tried.

SUBACUTE COMBINED DEGENERATION OF THE SPINAL CORD

This is a malady of middle-aged and elderly persons of both sexes, and presents the clinical picture of a progressive lesion of the posterior and lateral

columns of the spinal cord. It is associated with pernicious anæmia. Sometimes the cord lesion precedes the blood change and dominates the clinical picture, but in other cases the symptoms of a nervous lesion may occur during the course of a fully developed pernicious anæmia.

Ætiology.—The disease is uncommon before the fourth decade of life. Its ætiology is that of pernicious anæmia, to which the reader is referred (p. 266).

Morbid Anatomy.—The cord is normal in appearance on the surface, but on section the posterior and lateral white columns present the translucent appearance of degeneration. The foci of this change lie in the centre of the posterior column and deep in the posterior part of the lateral column. With the development of the disease they enlarge progressively until they reach the surface of the cord, and include all the white matter except that immediately surrounding the grey matter and containing the short proprio-spinal fibres.

Microscopically, demyelinisation and destruction of axis cylinders with the presence of vacuolisation, where fibres have been completely destroyed, constitute the essential lesion. There is strikingly little neuroglial or vascular reaction, a feature which distinguishes this disease from all other spinal cord diseases. The process is most intense in the thoracic segments of the cord, but extends up as far as the brain stem. The cell bodies of degenerated nerve fibres show secondary changes. In some cases considerable peripheral degeneration of the limb nerves may be seen, even greater in intensity than the cord changes.

Symptomatology.—The onset of nervous symptoms may be preceded by periodical gastro-intestinal disturbances: slight fever, diarrhœa alternating with constipation, pain in the hypochondrium, and occasionally jaundice. Attacks of this kind sometimes punctuate the course of the developed disease. The onset is usually slowly progressive, and the initial symptoms consist of subjective sensory disturbances in the extremities, especially in the feet. The patient complains of feelings of wetness, coldness, numbness, tingling, and of "pins and needles." Similar, but less distressing, paræsthesiæ may be present in the fingers, which begin to lose fineness of co-ordinated movement with their appearance. Pain below the costal margin of "girdle" character is common, and may become more marked during the febrile reactions associated with the occasional bouts of diarrhœa.

Examination at this stage reveals in many patients the peculiar colour of complexion and the shiny atrophic tongue of pernicious anæmia, though these signs may be absent. The blood may present changes identical with those of the various degrees of pernicious anæmia, but in many early cases very little deviation from normal may be found, although ultimately severe anæmia usually develops. It has been mentioned that achlorhydria is extremely common in subacute combined degeneration, but it is not yet possible to say that it is an absolutely constant finding. The spinal cord symptoms vary according to whether the posterior or lateral white columns are predominantly affected. Usually the former are earlier involved, but by the time definite symptoms appear the presence of a Babinski plantar response indicates lateral column affection. Two clinical types may be recognised:

1. *Flaccid Type.*—In this posterior column symptoms may predominate, namely, weakness and flaccidity of the lower limb muscles with some degree of sensory ataxy and of Rombergism, absence of the tendon jerks, and impairment of cutaneous sensibility of minor degree over the distal parts of

the limbs. The calf and plantar muscles are almost invariably tender to pressure, a clinical indication of the peripheral nerve degeneration which is always found on microscopic examination. In some instances the physical signs are—at least in the early stages of the malady—quite indistinguishable from those of a peripheral neuritis. Sooner or later, however, the appearance of a Babinski plantar response indicates the presence of spinal cord changes, while the associated blood changes help to distinguish the case from an ordinary one of peripheral neuritis.

2. *Spastic Type.* — In other cases lateral column signs predominate, namely, spastic weakness of the legs with increased tendon jerks, clonus and the Babinski plantar response. As the paralysis increases, painful and powerful flexor spasms make their appearance, and the final condition is one of paraplegia-in-flexion. Sometimes this symptom-complex gives place to that described above as the posterior columns are progressively involved. Variations of this kind, from case to case and from stage to stage in a given case, indicate the development of the process in the posterior and lateral columns of the cord, and so far from rendering diagnosis difficult constitute one of the most characteristic features of the malady.

As the disease advances, motor weakness and sensory loss increase, the patient becomes bedridden, and if anæmia be present the characteristic signs thereof are added to those of the cord lesion. As a rule the functions of the cranial nerves are unaffected. Slight œdema of the optic disc is occasionally seen, and retinal hæmorrhages may be a terminal phenomenon. If a severe grade of anæmia accompanies these nervous symptoms, mental disorder may make its appearance. Memory is defective, and the patient becomes irritable and confused. In extreme cases the patient may be delusional and difficult to handle. The cerebrospinal fluid is usually unaltered.

Prognosis.—It is not possible in the present advancing state of knowledge to make a definite statement as to prognosis. In many cases of pernicious anæmia in which appropriate treatment has restored the blood to an approximately normal condition, the signs and symptoms of a cord lesion have undergone no corresponding degree of improvement, and may even have increased in severity until the patient becomes paraplegic. On the other hand, in early cases, and especially those in whom the signs are those referred to above as resembling a peripheral neuritis, remarkable improvements may be achieved. The severely spastic cases, as might be expected, respond much less favourably and frequently not at all. The final stage of the disease is then one of profound cachexia with motor, sensory, and sphincter paralysis, and the various complications which arise from this state however produced.

Diagnosis.—In typical cases the clinical picture is so characteristic as to be readily recognisable. The patient is over forty years of age, yellowish in colour with a malar flush, pale mucosæ, and a shiny tongue, though these signs are not constantly present. The signs of a postero-lateral degeneration of the cord complete the picture. When anæmia is absent, and the picture of spastic paresis of the legs is present, disseminated sclerosis can generally be excluded by the age of the patient, the presence of cutaneous sensory loss, and absence in the history of the visual symptoms which often occur early in the course of disseminated sclerosis. Moreover, the prominence of paræsthesiæ in subacute combined degeneration is rarely a feature of disseminated sclerosis. With absent tendon jerks and flaccidity of the lower limb muscles, tabes may be excluded by the absence of the tabetic pupillary abnormalities,

of the sensory loss on face and trunk, and by the presence of muscular tenderness in place of the muscular insensitiveness to pain of tabes. The cerebro-spinal fluid also renders the recognition of tabes possible. A slowly developing polyneuritis may more closely resemble an early subacute combined degeneration with posterior column involvement predominating than either of these maladies, and in the absence of an extensor or Babinski type of plantar response, differentiation may for a time be difficult until the progress of the malady reveals signs of lateral column degeneration.

Treatment.—Whether the blood picture be certainly that of pernicious anæmia or not, the treatment of subacute combined degeneration of the cord is that of pernicious anæmia, *but more persistently and more intensively carried out*. The improvement in the nervous symptoms must be the sole guide in this respect, and no precise rules can be laid down. Intramuscular injections of a whole liver extract may be necessary daily for three or four weeks before a progressive improvement sets in.

As has been said, the spastic type of subacute combined degeneration frequently makes no response whatever to treatment, but the flaccid type, especially in its early stages, will often improve in a remarkable manner if treatment be continued over a long period, and "maintenance" doses of a liver extract be given from time to time.

Details of treatment are given under the heading of Pernicious Anæmia (*vide* p. 266).

If an anæmic patient respond to this treatment, the ataxy of gait and the weakness may be dealt with by carefully graded re-education exercises and by massage. In the terminal stages of the malady, sleeplessness, pain, flexor spasms in the legs, cystitis, and bedsores may all call for appropriate symptomatic measures.

THE HEREDO-FAMILIAL ATAXIES

This group of associated maladies includes several clinical types of motor disorder, which depend for their respective features upon a varying incidence of degenerative changes in the parenchymatous elements in cerebellum, brain stem, and cord. As the title of the group indicates, hereditary and familial factors are the rule.

Ætiology.—Direct or indirect inheritance is present in most instances, and several members of a family may be affected, both sexes being equally liable. The symptoms commonly make their appearance during childhood. Beyond these simple facts of observation nothing is known of their causation, but it is probable that a developmental defect is responsible.

Morbid Anatomy.—Usually, there is no macroscopic abnormality of the nervous system. The essential lesion is a primary neurone degeneration, with an associated secondary neuroglial reaction. In the spinal cord, the posterior column fibres and the two spino-cerebellar tracts on the afferent side, and the pyramidal tract on the efferent, are the neurone systems most commonly affected. In the brain, cerebellar neurones, both intrinsic and projection systems, cortico-spinal fibres, and retinal neurones are the systems usually involved. Not all these systems are involved in each type. Thus, in Friedreich's ataxy, the incidence of the lesion is in the posterior and lateral columns of the cord, while in certain forms of cerebellar ataxy, cerebellar neurones alone present pathological changes.

The following clinical types are described :—

Friedreich's Ataxy.—A disease developing slowly during childhood, frequently affecting more than one member of a generation and characterised by the signs of progressive degeneration of posterior column, pyramidal and spino-cerebellar fibres, and by certain skeletal deformities.

Ætiology.—It commonly makes its appearance during the second five years of life, but may not do so until adult life is reached. It tends to develop progressively until the subject is disabled, but its course may be arrested in the early stages before gross disability is produced. While the malady is commonly reported in generations preceding the one which comes under observation, single cases occurring in a stock otherwise free from all trace of nervous disease may occur.

Morbid Anatomy.—Degeneration of the exogenous fibres of the posterior columns and of pyramidal and spino-cerebellar fibres with resulting sclerosis of the posterior and lateral columns are found. There may also be degenerative changes in the cells of Clarke's column (nucleus thoracicus).

Symptomatology.—The symptoms of the disease are the natural result of a lesion of the fibre systems named above. In the legs are found the characteristic signs of postero-lateral cord degeneration, namely, weakness and flaccidity of the musculature, absence of the tendon reflexes, the extensor type of plantar response, and impairment of the sense of position with a corresponding degree of sensory ataxy.

In the arms, signs referable to disturbance of cerebellar function predominate, namely, tremor and unsteadiness of movement.

The arms and head show fine jerky movements when the muscles which innervate the limbs and neck are in action. Similarly, the facial and articulatory musculature may be affected with the production of facial twitching and disorder of articulation. A fine nystagmus is the rule.

All these symptoms develop insidiously. At first the child becomes unsteady on its feet, tends to stumble and fall, and to have difficulty in changing position. In some cases the child has never been normally nimble on its feet from early childhood. Later, the gait becomes markedly unsteady and the arms also show disorder of movement.

In addition to these indications of nervous disorder, certain skeletal deformities are the rule : kypho-scoliosis of the thoracic spine and pes cavus. A rare symptom is optic atrophy with visual defect. Other congenital anomalies have been recorded such as congenital morbus cordis.

The course of the disease is usually very slowly progressive, although, as has been stated, arrest may occur at any stage. Death usually results from intercurrent maladies after the patient has become disabled and bedridden.

Treatment.—The course of the malady is not materially influenced by any mode of treatment, but its progress may be delayed and the final stage of complete disability may sometimes be put off by careful massage and remedial exercises.

Hereditary Cerebellar Ataxy.—This comparatively rare malady develops somewhat later in life than Friedreich's ataxy, occasionally in a family one member of which presents the latter disease, and resembles it pathologically and clinically in certain respects. Thus there is degeneration of the spino-cerebellar and pyramidal fibre systems, as in Friedreich's ataxy, but also degeneration of neurones within the cerebellum. Clinically, the same signs of cerebellar disturbance are seen, namely, nystagmus, articulatory

disorder, tremor and ataxy, and in the lower limbs the phenomena of spastic weakness with their appropriate reflex alterations. Primary optic atrophy may occur.

Cerebellar Atrophy.—There are two forms of this primary cerebellar degeneration : (i) cortical atrophy, and (ii) atrophy of the white matter (the so-called olivo-ponto-cerebellar atrophy). These are not always familial.

Clinically, these are usually indistinguishable, and consist of a gradually increasing cerebellar ataxy involving the limbs and the musculature of articulation. Nystagmus may be absent. The patient is commonly a middle-aged or elderly adult. The malady is slowly progressive and does not respond to treatment.

PROGRESSIVE MUSCULAR ATROPHY

General Considerations on Muscular Wasting.—Muscular atrophy may result from disease primarily affecting the muscle fibre itself, or from disease of the motor neurone innervating it. In the differential diagnosis of the various clinical conditions which present muscular wasting the following factors are of importance : (1) the mode of development and the distribution of wasting ; (2) the presence or absence of certain peculiarities in the wasting muscle (fibrillation, tenderness, changes in direct and electrical excitability) ; (3) the presence or absence of signs of co-existing disease of the nervous system ; and (4) the presence or absence of heredo-familial factors.

Cases of muscular atrophy fall into four main groups : (i) primary muscular dystrophy (myopathy) and certain allied conditions ; (ii) progressive muscular atrophy of spinal origin ; (iii) muscular atrophy secondary to paralysis of nervous origin ; (iv) atrophy of muscles following arthritis.

The differential criteria given above may now be considered in detail.

1. *Mode of Development and Distribution.*—Speaking generally, the wasting of muscular dystrophy and of progressive muscular atrophy are very slowly progressive, the weakness being a result of the wasting. In post-paralytic atrophy weakness precedes wasting, and may be sudden in onset, while the wasting is more gradual. Bilateral symmetry of wasting is characteristic of muscular dystrophy. In progressive muscular atrophy the wasting, although bilateral and often symmetrical in incidence, is rarely symmetrical in degree, since wasting appears in one limb earlier than in its fellow, and remains more advanced in the earlier affected muscles. When wasting of the intrinsic muscles of one hand remains unilateral for more than a year, the presence of a cervical rib may be suspected. Of equal significance is the incidence of the wasting throughout the musculature generally. Thus in muscular dystrophy the muscles of the limb girdle and the proximal limb segment are predominantly and often exclusively affected, while in progressive muscular atrophy wasting commonly begins in the distal limb muscles and remains most intense in these. Again, in muscular dystrophy the face muscles are often affected, but those of deglutition, respiration, and phonation escape. The reverse is the rule in progressive muscular atrophy.

In arthritis the muscles affected are those proximal to the joint, and particularly the joint extensors, *e.g.*, the vasti in arthritis of the knee-joint.

2. *Features of the Wasting Muscles.*—The irregular clonic twitchings of small muscle fibre bundles known as fibrillation are a prominent feature in progressive muscular atrophy, inconstant and slight in peroneal muscular

atrophy and post-paralytic atrophy, and absent in muscular dystrophy. In muscular dystrophy and progressive muscular atrophy the wasted muscles are painless on pressure; in wasting, secondary to a lesion of a peripheral motor nerve they are commonly extremely tender to pressure while wasting is in progress. In muscular dystrophy the mechanical and electrical excitability of the muscles wane progressively and finally disappear, without the latter undergoing any qualitative change. In progressive muscular atrophy and in post-paralytic wasting the mechanical excitability is increased, and at a certain stage of wasting the reaction of degeneration may be present. In muscular dystrophy alone the association of wasting and enlargement of different muscle groups is seen, the enlargement (pseudo-hypertrophy) being due to fatty and fibrous infiltration of the muscle.

In two muscular diseases, dystrophia myotonica and Thomsen's disease, a condition of myotonus or delayed relaxation is seen.

3. *Signs of Nervous Disease.*—Apart from an inevitable disappearance of tendon reflexes in wasted muscles there are no signs of nervous system involvement in muscular dystrophy, but such signs are found in progressive muscular atrophy and in post-paralytic atrophy.

4. *Age and Heredo-familial Factors.*—Muscular dystrophy commonly begins in infancy, childhood, or adolescence. Progressive muscular atrophy is a disease of adult life. In the latter heredo-familial factors are absent, but are constant in muscular dystrophy.

Motor Neurone Disease

Progressive Muscular Atrophy, Chronic Bulbar Palsy, and Amyotrophic Lateral Sclerosis.—Under these headings are described a single pathological process consisting in a primary degeneration of motor cells of the anterior horns of the cord, or of certain cranial nerve nuclei, and also in a degeneration of the lateral white columns of the spinal cord. The clinical picture varies according to the incidence of the motor cell degeneration, and also according to the relative degree of lateral column degeneration. In some cases the latter may not be evident clinically, while in others it dominates the clinical picture. Three main clinical types of the malady are described, but mixed types occur.

Ætiology.—Rarely the disease may develop in the second decade of life, but the greatest frequency of case incidence is in the fourth decade. Males are more frequently affected than females, and this predominance increases with the age of onset. Its causation is quite obscure, and as is common in such circumstances, trauma is sometimes invoked as a causative factor but without conclusive evidence. A comparable clinical picture is sometimes produced by syphilis, but syphilitic amyotrophy runs a somewhat different course, and is generally distinguishable both on clinical and serological grounds.

Morbid Anatomy.—There are no striking macroscopical abnormalities in brain or spinal cord. The latter, seen in a section stained by the Weigert method, shows pallor of the lateral columns, particularly of the pyramidal tracts, and some change of this kind is seen even in cases which, during life, presented no clear signs of pyramidal tract involvement.

By the Nissl method the motor nerve cells in the affected regions are found to be diminished in number, the remaining cells being shrunken and

altered in form and appearance. A slight degree of secondary neuroglial proliferation may be seen. Similar changes are found in the cranial nerve nuclei when the incidence is bulbar, while the Betz cells of the cerebral motor cortex may also be involved. The wasted muscles show all degrees of muscle fibre atrophy.

Symptoms.—When the symptoms are referable, wholly or almost so, to degeneration of cells in the cervical segments of the cord, we speak of *progressive muscular atrophy* ; when there are signs of an associated lateral column sclerosis we speak of *amyotrophic lateral sclerosis*, while in the case of a bulbar incidence of the nerve cell degeneration we speak of *chronic bulbar palsy*. This differentiation of the malady into three clinical types is artificial, since a given case may present signs of all three, and this in varying proportion. In simple progressive muscular atrophy, so called, wasting usually makes its first appearance in the intrinsic muscles of one hand. This wasting is sometimes preceded by transient local aching pains and by paræsthesiæ. The wasting may advance slowly up the limb, involving successively the shoulder girdle and scapular muscles, including the lower half of the trapezius, the rhomboids, serratus magnus (S. anterior) and latissimus dorsi, and finally the neck muscles, including the sternomastoid and the muscles of respiration. Weakness follows wasting and is in proportion to the degree of the latter.

The wasting muscles fibrillate freely and their mechanical irritability ("tap contraction") is greatly increased, and the reaction of degeneration may be present. The interval between the involvement of the two arms is generally a matter of several months, but usually less than one year. The progress of the disease varies from case to case. The wasting may become arrested before the region of the shoulder girdle is invaded, or, on the other hand, progress may be rapid and involvement of the neck and respiratory muscles may result in death within two years from the apparent onset of the malady. The degree and extent of the fibrillation generally gives some indication as to which of these two courses the malady is likely to run in a given case, free and widespread fibrillation, involving muscles not yet wasting, being of bad prognosis.

Chronic Bulbar Palsy.—This is the expression of a degeneration of the motor cranial nerve nuclei, identical with that which may occur in the cervical region of the spinal cord. It is seen more frequently in males during the fourth and fifth decades of life. From the topography of the paralysis it is often spoken of as "labio-linguo-laryngeal" or "labio-linguo-pharyngeal" palsy. The onset and progress are slow. The tongue is earliest and most severely affected. An indistinctness and laboured quality of the articulation is the first symptom and may at the onset appear only on fatigue. Later, the mobility of the tongue and lips becomes deficient, the tongue shrinks, becomes wrinkled, and fibrillates freely. The laryngeal and suprahyoid muscles and those of the soft palate are later involved. The articulation becomes unintelligible and the voice weak and nasal in quality. Weakness of the lips and of the soft palate allow dribbling and regurgitation of fluids through the nose, and when the pharyngeal muscles are affected deglutition becomes difficult. In these circumstances particles of food are apt to enter the glottis, with the production of an aspiration pneumonia and death. This symptom-complex may exist alone or be associated with the wasting of the limbs already described ; the bulbar symptoms may usher in the disease or be a late complication.

Amyotrophic Lateral Sclerosis.—One or both of the above clinical pictures may be associated with signs of sclerosis of the lateral white columns of the cord and of pyramidal fibres in the brain stem. These signs predominate in the lower limbs, which may become spastic, with increased tendon jerks, clonus, and a Babinski type of plantar response. The most common clinical form of the disease is that in which wasting of the upper limbs and spastic paresis of the lower limbs are combined. Either group of symptoms may usher in the malady. It is probable that most cases of so-called primary lateral sclerosis are examples of this disease, in which lateral sclerosis antedates progressive muscular atrophy in the arms. Although wasting and fibrillation predominate in the arms, signs of lateral sclerosis involving the upper limb musculature in its consequences are seen in increased tendon jerks and increased mechanical irritability. The brisk jaw jerk so frequently seen in amyotrophic lateral sclerosis is another sign of pyramidal tract sclerosis.

Unlike what is found in certain other diseases in which the pyramidal tracts are the seat of change, the abdominal reflexes are not abolished early in amyotrophic lateral sclerosis.

Most difficult of diagnosis are those cases of progressive muscular atrophy with bulbar symptoms in which wasting of the lip, tongue, laryngeal and pharyngeal muscles is minimal, but phenomena of impaired upper motor neurone function predominate. Here the tongue is small and spastic, there is a tendency to emotional overaction of the face musculature, and wasting in the upper limbs is slight. Such cases somewhat resemble the condition known as pseudo-bulbar palsy, but the gradual onset and the clinical course with ultimate development of muscular wasting generally serve to exclude the latter.

Prognosis.—In all except a few cases of the cervical cord variety, where arrest may occur, the disease steadily progresses, and ultimately proves fatal from pulmonary complications within three years from onset.

Treatment.—There is no treatment which materially influences the course of the disease in any of its clinical varieties. Strychnine and the use of electrical stimulation of the affected muscles are useless, and, indeed, the latter may be harmful and there is no justification for its use. The avoidance of fatigue and all forms of stress and the maintenance of the general health are all that can be profitably attempted. The administration of vitamins E and B_6 has no value in either motor neurone disease or muscular dystrophy. In bulbar palsy the patient has least difficulty with semi-solid food. Even in cases of syphilitic amyotrophy arrest of the progress of the wasting is generally the best that can be hoped for. Circumstances often make the assumption of the passive role in treatment thus indicated very difficult to maintain, but it must be remembered that the adoption of active local measures, such, for example, as electrical stimulation, does little but exhaust the patient.

Progressive Spinal Muscular Atrophy of Children (Werdnig-Hoffmann).—The ætiology of this relatively uncommon disease is unknown. It may occur in several members of a generation, and both sexes are equally affected. It develops from birth or during the first six months of life.

Symptoms.—The apparently healthy infant begins to lose power, the trunk and proximal limb muscles being most severely affected. The reflexes are abolished, and electrical excitability of the muscles disappears. The sphincters are unaffected and there is no sensory disturbance or mental deterioration.

Death takes place within from three to five years. The lesion is an atrophy of the ventral horn cells and of the ventral nerve roots. The malady is uninfluenced by treatment.

PERONEAL MUSCULAR ATROPHY

(Neuritic, or Charcot-Marie-Tooth Type)

This disease is a form of slowly progressive muscular wasting of characteristic distribution. It is both familial and hereditary and makes its appearance in one of the first three decades of life, most commonly towards the end of childhood. Males are more frequently affected than females. It may first become manifest after an acute specific fever. Its ætiology is unknown.

Symptoms.—Wasting first develops in the plantar muscles and then in the peronei, long extensors of the toes, and calf muscles; later the muscles of the lower third of the thigh are affected. When the malady has been present for some years, wasting may make its appearance in the small hand muscles; ultimately both feet and hands become deformed. The wasting first invades the distal part of a muscle and later extends to its proximal portion. In this way, when the lower third of the thigh is wasted, the limb above the knee assumes the form of an inverted Indian club.

The wasting is frequently but not constantly bilaterally symmetrical. The progress is so extremely slow that the subject may reach middle age before being seriously disabled. Fibrillation in the affected muscles may be seen but is never marked.

The ankle jerks disappear as the calf muscles become involved, and later the knee jerks also disappear. There may be impairment of all forms of sensation over the wasted territory of the limb.

The disease does not shorten life and is not amenable to treatment, though the foot-drop may call for mechanical support.

Morbid Anatomy.—There is degeneration of the posterior white columns of the cord and also of anterior horn cells, the anterior nerve roots are shrunken, and the branches of the peroneal nerve may show some interstitial neuritis.

MUSCULAR DYSTROPHY

(Myopathy)

Under this heading we deal with a condition in which the skeletal muscles from congenital defect and progressive pathological change undergo atrophy. There is no associated lesion of the nervous system, and the disease is a primary one of the muscles themselves.

Ætiology.—It is of unknown ætiology, but may be of the nature of a qualitative defect in the embryonic tissue in which differentiated muscle fibres arise. It commonly occurs in several generations of a family and in the members of one generation. The malady may be transmitted by either sex and may occur in either. The pseudo-hypertrophic variety predominates in males, but the other varieties are more equally distributed between the sexes.

Morbid Anatomy.—The muscle fibres are diminished in number and the interstitial tissue is increased in some muscles to such a degree that little or no contractile tissue remains. In the enlarged muscles fat globules are

deposited in the fibrous tissue. Microscopically, the muscle fibres are shrunken, vacuolated, and altered in form, and their nuclei are increased in number.

Symptomatology.—The malady develops during infancy or childhood. It is slowly progressive, and although in the pseudo-hypertrophic form some of the muscles are enlarged, the general progress is towards wasting of the affected muscles. The initial symptoms vary according to the clinical variety of the disease present. In many cases the child has never been normally nimble on its feet, and may have learned to walk and stand unduly late. Attention is called to the condition by the child's waddling gait, its tendency to fall, with a resulting difficulty in regaining the erect posture. In these circumstances the child rolls over on to his face, gets on to hands and knees, and then proceeds to climb up its legs by moving the hands alternately upwards on the limbs. Weakness of the hip extensors and contracture of the flexors lead to the adoption of an extreme lordosis, and weakness of the shoulder girdle muscles to winging of the scapulæ.

Certain muscles are constantly affected. These are the lower part of trapezius and of pectoralis major, latissimus dorsi, serratus magnus (S. anterior), biceps and triceps, and in the lower limbs the adductors and hamstrings. When pseudo-hypertrophy is present it involves erector spinæ, the masseters, deltoid, spinati, sometimes biceps and triceps, and in the lower limbs the calf muscles, vasti, and glutei. Both wasted and enlarged muscles are weak, and the weakness is in proportion to the degree of atrophy of contractile tissue. The mechanical and electrical excitability of the affected muscles progressively wane and disappear, the electrical excitability undergoing no qualitative change such as the reaction of degeneration. Fibrillation does not occur. Ultimately, kypho-scoliosis and contracture and deformity of the legs develop in the pseudo-hypertrophic form of the disease. The tendon jerks become enfeebled and disappear as the relevant muscles waste. There is no sphincter defect and no sensory change. The following clinical varieties are recognised, but mixed forms are common.

Pseudo-hypertrophic Type.—This is usually seen in males, is the commonest type, and develops during the first decade of life. The subjects do not reach adult life, becoming bedridden within a few years of onset and succumbing to some intercurrent disease, generally to pulmonary or intestinal infections. A waddling gait and enlargement of the calves may first attract attention to the child. The topography of wasting and pseudo-hypertrophy have already been stated.

Scapulo-humeral (Erb's) Type.—This occurs in children and adolescents of either sex. It is more slowly disabling than the pseudo-hypertrophic variety, and the patients reach adult life. Weakness of the shoulder and then of the pelvic girdle muscles, with winging of the scapulæ and lordosis and with wasting of the muscles concerned, are the features of this variety. Occasionally some enlargement of muscles is seen.

Facio-scapulo-humeral (Landouzy-Dejerine) Type.—This resembles the preceding type, but in addition there is marked weakness of the facial musculature, with thickening and eversion of the lips. The eyelids cannot be closed nor the teeth covered.

Distal or Simple Atrophic Type.—This relatively rare type differs from those described above in that the incidence is in the distal limb muscles mainly, the facial muscles being affected later.

In all forms the ocular, lingual, laryngeal, and pharyngeal muscles are intact.

Diagnosis.—The factors governing differential diagnosis have been stated in the chapter dealing with Progressive Muscular Atrophy (*vide* p. 688).

Prognosis.—Recovery is unknown in any form of myopathy. In general it may be stated that the earlier in life the condition appears the more rapidly does it progress. The usual termination is from some pulmonary complication. In the pseudo-hypertrophic type the patient does not reach adult life, becoming bedridden and dying within five or six years of the onset. In the other types, progress is much more gradual and adult life may be reached.

Treatment.—From what has been said above, it is clear that no material influence is exerted on the malady by any form of treatment. Attention may most profitably be directed to retarding the development of contracture and deformity by means of massage and of such active exercises as the patient may be capable.

Myatonia Congenita (*Amyotonia Congenita*)

A rare disease of infancy, thought by some authorities to be identical with the simple atrophic variety of muscular dystrophy, but differing from this in that there is a tendency to gradual and partial recovery. It is undoubtedly a familial and possibly an hereditary malady, certainly closely allied to myopathy. The new-born child has small and extremely soft muscles, which render possible an abnormal range of passive mobility of the limbs. There is no wasting and no associated signs of nervous lesion.

The child is not able to sit up or to hold its head erect until the second year of life, and may never be able to stand or walk. Occasionally, however, the capacity to do this may develop. The malady is not amenable to treatment.

Myotonia Congenita (*Thomsen's Disease*)

A very rare heredo-familial disease of obscure nature and origin, characterised by a peculiar tonic spasm and delayed relaxation of the muscles on voluntary effort. The only discoverable lesion is an enlargement of the muscle fibres, which are poorly striated. It develops during childhood, and the myotonia is always maximal on resuming activity after rest. There is not much weakness and sometimes the muscles may be enlarged, assuming herculean proportions. All the skeletal muscles may be affected. Its progress is extremely slow, and there may be some degree of associated mental impairment. It is not amenable to treatment.

Myotonia Atrophica (*Dystrophia Myotonica*)

A rare heredo-familial disease of unknown ætiology, developing during early adult life and occurring usually in males. It is characterised by atrophy of the facial muscles, of sternomastoid, of the forearm, hand and leg muscles, and also by myotonia, which is best and most constantly seen in the facial and tongue muscles, in the flexors of the forearm, and in the calf muscles. Percussion or electrical stimulation of the myotonic muscles evokes a slow localised contraction and delayed relaxation of the muscle fibres. Voluntary contraction is also followed by the same delayed relaxation. The patient has

a myopathic facies, with considerable weakness of the facial musculature. Associated with these symptoms are mental deterioration, premature baldness, cataract, and atrophy of the testicles. There is usually a history of presenile cataract in the generation immediately preceding the myotonic generation, and of senile cataract in the second generation. The myotonic generation, therefore, is the third abnormal generation in the family. A myotonic individual has, however, been known to become the father of a healthy child. It is clear from the wide range of symptoms that something more than a purely muscular disease is in question, and it is probable that we are dealing with a degenerative disease, developing over more than one generation and involving other structures than the musculature. Of its morbid anatomy little is known. Quinine in 5-gr. doses twice or thrice daily reduces the myotonia appreciably.

Family Periodic Paralysis

This is a rare heredo-familial malady developing in childhood or adolescence, and characterised by attacks of paralysis affecting mainly the thoracic and proximal limb muscles. These often come on during the night or during periods of rest, and reach a maximum within a few hours, passing off again after a similar interval. As weakness develops, the tendon reflexes and the electrical excitability of the muscles wane and disappear. Consciousness and sensation are unimpaired. An occasional ptosis is the only sign of muscular involvement within the distribution of cranial nerves.

Death is reported to have occurred during an attack. Potassium chloride in 10 to 15 gr. doses will avert or cut short an attack.

MYASTHENIA GRAVIS

Although there is rarely any muscular wasting in this malady it may appropriately be considered here, since the constant feature in its symptomatology is a disturbance of muscular power without discoverable nervous system disease. There are no heredo-familial factors.

Ætiology.—It is of unknown ætiology, is slightly more common in women than in men, and develops during adolescence or early adult life, though rarely an onset in elderly persons is seen. Occasionally it coexists with exophthalmic goitre. There is reason to think that the essential disorder in this disease has its seat in the neuromuscular junction. When the nerve impulses reach this junction acetylcholine is liberated and renders the muscle fibres sensitive to the nerve impulse. But if this substance be not liberated, or if it be prematurely destroyed, muscular contraction either fails or is ineffective.

One or other of these abnormalities is probably present in myasthenia gravis. It has been found that the injection of physostigmine (or of the synthetic product prostigmin) will temporarily abolish this defect and cause the complete—or almost complete—disappearance of all the symptoms of myasthenia gravis in a very dramatic fashion, the effect lasting for two or three hours. Where diagnosis is uncertain, this fact provides us with a diagnostic test. Four cubic centimetres of prostigmin with $\frac{1}{100}$ gr. of atropine sulphate (to check the peristalsis which would otherwise occur) are injected

hypodermically, and in about half an hour the patient's muscular condition is approximately normal, and so remains for a few hours.

Morbid Anatomy.—An enlarged persistent thymus is commonly but not constantly found. Small foci of mononuclear cells (lymphorrhages) are found in the muscles, especially the oculomotor muscles, the liver, and the myocardium. Occasionally there may be some muscular atrophy with degenerative changes in the muscle fibres. Nothing is known of the significance of these changes.

Symptoms.—The essential symptom is the rapid development of fatigue and transient paresis in voluntary muscles. Muscles supplied by both cranial and spinal nerves are affected. The extrinsic ocular muscles are almost constantly affected in varying degree, and in a given case may for long periods be exclusively involved. Ptosis, variable squints, and diplopia, dropping of the jaw and weakness in mastication, weakness of phonation, articulation, and deglutition may all occur, and any of the trunk and limb muscles may be similarly affected. In severe cases the least exertion may produce a transient weakness of the muscles employed and render the patient incapable of any activity. In some instances the muscular affection is severe and widespread, and death may occur within a few months of onset from failure of the respiratory muscles. In other cases the malady runs a chronic course, and in these the ocular muscles are predominantly or even exclusively affected, and permanent paralysis of ocular movement may result. If this involve all the ocular muscles the eyes come to rest in the median position and diplopia disappears.

Occasionally the pupillary reactions are defective, while ptosis may be replaced by lid retraction and some exophthalmos.

Striking variations in the clinical course of the malady occur, and patients apparently in grave danger of respiratory paralysis may regain power and remain for long periods free from symptoms. Faradic stimulation also temporarily exhausts the muscle, which may cease to react for some seconds. Usually the tendon jerks remain active and inexhaustible.

Diagnosis depends largely upon the variability of the symptoms, upon their increase by exertion, and by the absence of qualitative change in the reflexes or of sensory loss.

Prognosis.—As has been said above, the malady may prove rapidly fatal, may undergo apparent arrest or long remission, or may become localised to the ocular muscles and remain chronic over a long period of years. It is probable that the younger the patient and the wider the involvement of limb and trunk musculature, the worse the prognosis as to duration of life.

Treatment.—The patient's exertions should be within the limits of fatigue. The medicinal treatment consists in the administration of prostigmin, and experience shows that larger doses can be given than was formerly thought possible. Orally, from four to twelve or even more tablets of 15 mg. can be given in the twenty-four hours, so spaced as to make the taking of meals easy for patients who have difficulty in masticating. Hypodermically the dose is 1 to 2 mg., and this may be combined with atropine sulphate ($\frac{1}{100}$ gr.) to prevent peristalsis. In critical cases, prostigmin may be given as a slow drip. Within the past few years the operation of thymectomy has been performed. This gives best results in early cases with simple thymic enlargement. It is too early to assess the value of this procedure.

POLYNEURITIS

(Multiple Peripheral Neuritis)

Under these titles we are concerned with a strikingly uniform reaction of the nervous system to various poisons which also simultaneously affect the heart muscle. While the damage suffered by the peripheral nerves is responsible for the clinical manifestations of polyneuritis, the central neurones of brain and spinal cord do not escape, and themselves present pathological changes. With certain exceptions it is the functions of the spinal nerves which are affected, and one of the features of the condition is the bilateral symmetry of the paralyses and other symptoms. The essential lesion is a parenchymatous degeneration of the nerve fibres.

Ætiology.—Despite the apparent diversity of the poisons which give rise to it, polyneuritis displays a remarkable clinical and pathological uniformity. A wide range of chemical substances, from arsenic to alcohol, and such complex substances as the exotoxins of diphtheria may give rise to it; while it develops in typical form in such metabolic disturbances as beri-beri and diabetes. Finally it is not uncommonly encountered when no discoverable cause is operative. In these circumstances we may ask whether these diverse agencies do in fact act directly upon the nervous system to produce a single mode of reaction, or whether they may perhaps do so indirectly, and in virtue of a common disorder of metabolism induced by them; a disorder in the course of which a single toxic metabolite is produced in the body to become the direct neural and myocardial poison. We cannot yet say that such an hypothesis covers every ætiological variety of polyneuritis, but there is evidence suggesting that many varieties are so induced: *e.g.*, beri-beri, alcoholic polyneuritis, and the polyneuritis which is occasionally seen in gastric ulcer or carcinoma or in hyperemesis.

Carbohydrates are essential to the metabolism of nerve cells, and vitamin B_1 is essential to their oxidation within the cell. In the absence of this vitamin this breakdown in the nerve and cardiac cells is arrested at the stage of pyruvic acid formation, and it is conceivable that this substance is toxic for the nervous system. It has to be remembered, however, that in beri-beri, the best established example of B_1 avitaminosis, the symptoms and the lesions are referable not to nerve cells in the brain but to the axis cylinders of peripheral nerves. Therefore, it is evident that the chain of processes leading to the development of a polyneuritis in the presence of vitamin B_1 deficiency still contains undiscovered links.

It has been suggested that vitamin B_1 deficiency may arise either from deficient vitamin intake (as in beri-beri) or from defective absorption of vitamins in the alimentary canal (as in gastric ulcer and hyperemesis).

However, whatever the facts may ultimately prove to show, there remains a considerable residue of cases of polyneuritis, both acute in onset and of gradual development and chronic course, in which in the present state of knowledge it is impossible to invoke any mode of avitaminosis. Such are the varieties of polyneuritis known as Landry's paralysis, acute febrile polyneuritis, and a more chronic variety often associated with some papillœdema, and a great increase of protein in the cerebrospinal fluid. These are found to occur in subjects apparently healthy, adequately nourished, and free from all discoverable infections.

In short, the problems of polyneuritis are still far from complete solution.

It is customary to include lead among the metallic poisons producing polyneuritis, but both clinically and pathologically the nervous affections arising from lead poisoning differ from polyneuritis, and therefore lead paralyses will be dealt with separately. This applies also to the clinico-pathological phenomena associated with other chemical poisons, such, for example, as carbon disulphide.

The symmetry with which the peripheral nerves, mainly those innervating the limbs, are involved in polyneuritis, and the associated myocardial affection justify the assumption that the various poisons concerned circulate in the blood stream and gain access to the nervous system from this source, but in the case of one form of polyneuritis, namely, diphtheritic paralysis, there occur certain " local paralyses " which suggest another possible channel of access of poisons to the neurone, namely, the perineural lymphatic space.

Morbid Anatomy.—The essential lesion in the peripheral nerve fibre is a parenchymatous degeneration, most intense at its distal part. The myelin sheath is most severely damaged, being broken down into fat globules. The axis cylinders are degenerated, and there is proliferation of the cells of the sheath of Schwann. A less severe degree of fibre change and some nerve cell change is also seen in the brain in long-standing cases. In fatal cases the heart muscle shows fatty infiltration and myocardial degeneration.

Cerebrospinal Fluid.—This usually shows no abnormality, but a slight increase in the protein content is sometimes found. Rarely the increase may be considerable and the fluid of a yellow colour.

Symptoms.—The following description applies to the polyneuritis of alcohol, arsenic, and of organismal toxins, with certain qualifications to be given later. The onset is insidious. For weeks or even months before disability ensues the patient complains of painful cramps in the calf muscles at night and of aching in the leg muscles on exertion. There are also tingling and subjective numbness of the extremities. Examination at this stage reveals tenderness of the limb muscles to pressure, especially of the calf and plantar muscles, slight blunting of all forms of cutaneous sensibility over the feet, and occasionally over the hands. The arm jerks are generally brisk, and the knee jerks also, but almost invariably there is diminution or loss of the ankle jerks. As the malady progresses weakness develops in the muscles below the knee, foot-drop becomes evident and gives rise to the so-called " steppage " gait in which the patient overflexes the leg in walking to clear the ground with the dropped feet. This phenomenon is not so much due to a selective weakness of the dorsiflexors as to the natural dropping of the foot under gravity, and examination will reveal that plantar flexion is also weak. With progressive weakness the patient is ultimately confined to bed and muscular wasting appears. The arms are similarly but often later and less severely involved. Simultaneously with these motor changes the tendon jerks in arms and legs finally disappear, and loss, or rather impairment, of all forms of sensibility develops. This last, like the weakness and wasting, is most profound over the distal segments of the limbs. When loss of the sense of position is marked before weakness takes the patient off his legs, Rombergism and ataxy of gait make their appearance. Only in exceptional and very severe cases does weakness or sensory loss invade the trunk. Sphincter control remains intact. If the condition be allowed to progress, profound wasting of limb muscles with fibrous contracture and deformity develop.

Foot-drop is thus rendered a permanent deformity, and the legs tend to become fixed in flexion. Trophic and vasomotor disturbances are present and of a severity proportionate to the motor and sensory disturbances. The skin of the feet becomes cyanosed and clammy and may perspire freely. The skin of the fingers becomes shiny and thin and the nails curved and rigid.

Pain in the affected muscles and cutaneous hyperalgesia may be extreme. In all developing and advancing cases of polyneuritis there are signs of myocardial involvement, of which, while the patient is bedridden, tachycardia and possibly some dilatation of the heart are the most constant. In the polyneuritis of diphtheria and in beri-beri there is a special liability to sudden fatal heart failure.

Alcoholic Neuritis.—In many chronic alcoholics there are to be found on examination the initial signs of a polyneuritis, which never develop fully. Characteristic of the polyneuritis due to this poison is the extreme tenderness of the muscles and the severity of the weakness and wasting seen in some cases. There may also be intense superficial pain and hyperæsthesiæ of the extremities. Bilateral facial weakness is sometimes seen.

Arsenical Neuritis.—Single massive doses of arsenic or repeated small doses, given therapeutically or otherwise, may produce polyneuritis. It has been known to occur from the free application of an arsenical paste to a large ulcer.

In cases in which single or repeated large doses have been given, a history of acute gastro-intestinal and cardiac symptoms may be obtained, and in these circumstances a mental state comparable to Korsakow's psychosis (*vide* p. 760) may occur. The general course and symptoms are similar to those described above. Wasting and contracture may be extreme, and the skin of the palms and soles shows a condition of hyperkeratosis, while on the abdominal wall there may be seen the characteristic arsenical pigmentation. In such cases arsenic may be identified in the skin, hair, and urine.

Diphtheritic Neuritis.—The sequence of events is rather different from that described above, and the clinical picture contains elements absent from the neuritis due to poisons other than the toxin of diphtheria. This difference, however, is entirely due to the fact that the poison gains access to the system from a strictly localised and peculiar focus, namely, from the fauces. At the end of the first or during the second week of diphtheria there may develop regurgitation of fluids through the nose, a nasal quality in the voice, and a defect of near vision. These phenomena are due to paralysis of the soft palate and to paralysis of accommodation, and they may persist for any period up to three or four weeks from the date of appearance. Sometimes ptosis, squint, and diplopia occur. No other nervous symptoms may develop in the patient, but in some cases at about the fifth or sixth week, and often as the palatal and ocular phenomena are clearing up, the patient develops a polyneuritis like that described above.

It differs, however, in some minor details. Its development is more rapid than that of the polyneuritis due to alcohol, and it very rarely leads to long-standing paralysis or wasting. In fact, diphtheritic paralysis is perhaps the only organic nervous disease in which the patient's relatives may with some confidence be given the assurance that complete and permanent recovery within from six to eight months will ensue; it is the commonest form of polyneuritis in children. From time to time cutaneous and wound infection by the diphtheria bacillus occurs, and may be followed by diphtheritic

paralysis. In such cases, however, the initial palatal paralysis is absent, and is replaced, though not in all cases, by an initial "local paralysis" of muscles at or near the site of the focus of infection. It is probable that while the polyneuritis is a blood-borne intoxication of the nervous system, the initial "local" paralyses are the result of an ascending perineural lymphatic infection.

Polyneuritis in other infections resembles the polyneuritis of diphtheria.

Diabetic Neuritis is due to the action of toxic substances produced during the course of an aberrant metabolism. It is rarely as severe as the forms that have been considered above but may be discovered in the routine examination of a diabetic subject. On the other hand, a form of peripheral neuritis characterised by severe ataxy and by intense pains in the legs like those of tabes dorsalis may occur during the course of diabetes. To this the name *pseudo-tabes peripherica* has been applied. Again, a sudden severe neuritis of a single nerve may occur, with resulting paralysis and sensory loss. The ulnar and anterior tibial nerves may be affected in these circumstances.

Beri-beri is also a form of toxic polyneuritis, the aberrant metabolism responsible in this case arising from the use of a diet lacking in vitamin B_1. Clinically and pathologically it resembles the forms described above, differing only in the presence in some cases and at some stage of their course of a generalised œdema.

Acute Febrile Polyneuritis (*Acute Infective Polyneuritis, Landry's Paralysis*).—It is probably a single condition that is referred to by these three titles. Following a brief and somewhat featureless febrile illness, a severe and rapidly developing polyneuritis develops, often with facial diplegia, and in fatal cases with a rapidly ascending paralysis of the trunk muscles leading to respiratory paralysis. When death does not ensue, the extent and severity of the paralysis tends to wane rapidly, though complete recovery may be delayed for some months. Pain and sensory loss are minimal in this variety.

Erythrœdema Polyneuritis (*Pink Disease*).—This is a disease of early childhood in which a short-lived febrile reaction is followed after a variable interval of from a day to two or three weeks by an acutely developing polyneuritis; with this is associated a bright erythematous rash, insomnia, anorexia, and marked mental dejection (*vide* p. 189).

Prognosis of Polyneuritis.—This necessarily depends upon the severity of the paralysis, the degree of wasting that has occurred and the presence of contracture when this has been allowed to occur. If in a case of acute onset treatment is adequately carried out from the outset, a virtually complete recovery can be looked for, though it will take close upon twelve months at least to secure. In the case of a relatively mild post-diphtheritic paralysis recovery may occur sooner than this, but the patient will probably not be ready to resume normal activity in less than six or nine months. The presence of deformity, of course, renders recovery slower and less perfect.

Treatment.—Even in mild cases in which no severe degree of paralysis is present, rest in bed is the first essential of treatment until improvement has definitely begun. The associated cardiac condition is another indication for rest.

There can be no doubt that a premature return to physical activity after mild and undetected diphtheria may be responsible for the development of

a polyneuritis which the subject might otherwise escape, and therefore, particularly in the mild cases of polyneuritis associated with infections, caution in this respect is most important. In severe paralysis the maintenance of a good position of the limbs is essential, and the legs should be kept extended, adducted, rotated in, and with the feet supported. When the forearm muscles are severely involved, similar precautions are necessary. The presence of pain may prevent any active manipulation or massage of the limbs, but this should be carried out when possible. Electrical stimulation of the muscles is of no value, and may do harm if strong currents are employed. In the matter of drugs, pain may require treatment by aspirin and allied compounds, but the morbid process cannot be directly influenced by drugs. General tonic treatment is indicated, and strychnine is a useful agent. In alcoholic cases some attempt may be made to deal with the addiction. Since it is possible that there is a common ætiological factor of a metabolic order underlying most or all forms of polyneuritis, and it has been shown experimentally that a diet defective in vitamins A and B_1 may lead to nerve fibre degeneration, the administration of these substances, therefore, is rational in polyneuritis. These may be given in severe cases in the form of vitamin B_1 concentrates in daily intramuscular doses from of 20 to 100 mg., continued as long as necessary. They may also be given in the form of yeast—half an ounce of baker's yeast daily—or as Marmite. It is, of course, not to be expected that the results will be as dramatic as have been recorded in the so-called experimental beri-beri of birds, and the use of these preparations does not dispense with the necessity for the other therapeutic measures already mentioned. Indeed, it cannot yet be said that the duration of the illness and of the ensuing disability have been lessened in polyneuritis since intensive vitamin B_1 therapy has become general.

Lead Paralysis and Encephalopathy

The general features of lead poisoning are dealt with elsewhere (p. 195), but we may say here that involvement of the nervous system may occur both in industrial and accidental poisoning with lead. When it occurs, the patient as a rule presents the general features of plumbism and gives a history of lead colic some weeks or months before the onset of nervous symptoms. The so-called lead palsy is the commonest nervous sequel of lead poisoning. The extensors of the fingers are first affected, then the extensors of the thumb, except the extensor ossis metacarpi pollicis (abductor pollicis longus) which may be little affected, and finally the wrist extensors. The supinator longus (brachio-radialis) commonly escapes, as does also the flexor group of muscles. "Wrist-drop" is the most striking result of this selective paralysis. In some instances there appears a slowly progressive wasting of the intrinsic muscles of the hands, associated with a corresponding degree of weakness. In severe cases the upper arm muscles may also be involved, deltoid, biceps, and brachialis anticus being most severely paralysed. Rarely, a similar condition may be seen in the legs.

In the subjects of chronic lead poisoning not presenting this characteristic picture of lead palsy, tremors, cramps in the muscles, and shooting pains in the limbs may be present.

Prognosis and Treatment.—The paralysis of the extensors under appropriate treatment, namely, rest in the position of relaxation and massage, may

completely recover, but the atrophy and weakness of the hand muscles tend to be persistent.

The ordinary measures, described elsewhere, for the elimination of lead from the system are employed (*vide* p. 197).

Lead Encephalopathy.—Disturbance of cerebral functions may also be a result of lead poisoning, and is indeed the common mode of nervous involvement in children. Convulsions, delirium, and coma coming on acutely, sometimes associated with fever and ending in death, may occur. Chronic cases also occur with recurrent convulsions and progressive mental deterioration. The character of the physical disturbances vary widely from case to case. Papillœdema and residual paralytic symptoms of hemiplegic character are common in the cerebral forms of plumbism.

SCIATICA, PROLAPSED INTERVERTEBRAL DISC, AND BRACHIAL NEURITIS

The two conditions discussed in this chapter are now less commonly thought of together than has formerly been the case, and this is because new views as to the ætiology and pathology of sciatica have gained ground, and these views have not so far been applied to brachial neuritis. This, it is here submitted, is unfortunate because sciatica and brachial neuritis have striking clinical features in common and it is unlikely that they can commonly have totally differing causes and pathology. The tendency now is to consider sciatica in a vacuum, as it were, but no sound balance of opinion can be looked for in respect of it, except on the general background of what we know of peripheral nerve and nerve root lesions.

Definition.—The problem of sciatica has been needlessly complicated by a deplorable vagueness as to what clinical condition we refer by the term, which has come to mean so many things that it is in danger of meaning nothing save the presence of pain somewhere in the buttock or lower limb. By the term " sciatica " we refer here to a painful malady, of acute or subacute onset, of relatively brief or prolonged course, in which accesses of pain are experienced along the course of the nerve—or part of this course ; in which the muscles supplied by the nerve are painful and tender to pressure and to stretching, as well as to the voluntary contraction involved in movement and the active maintenance of posture of the affected limb ; in which, in severe cases, there may be some wasting or even weakness in the muscles ; in which elevating the extended leg as the patient lies supine causes pain along the course of the nerve and in the stretched hamstring muscles ; in which the ankle jerk may be diminished or lost ; and in which there may be a sensation of numbness or objective sensory impairment along the outer side of the foot and leg. These purely neurological signs and symptoms may be accompanied by some rigidity of the lumbar spine, and, when standing, by a tilting upwards of the pelvis on the affected side with a compensatory scoliosis. This statement describes the fully developed clinical picture, but whether all or only some of its components are present depends upon the stage and severity of the cases. It will be seen from the foregoing that sciatica is thus essentially a neurological malady and not a simple matter of pain in the limb arising from joint, ligamentous, or muscular lesions not directly involving the nerve or its component roots.

Ætiology and Pathology.—There is no general agreement as to the causal factors in sciatica. The old view was that the essential lesion is an inflammation of the nerve sheath—an interstitial neuritis—and observers have described thickening and vascular congestion of the sheath with œdema of the nerve. It must be confessed, however, that since sciatica is a non-fatal malady it has never been possible to establish firmly the reality of this pathological process. More recently, rupture of an intervertebral disc, between fourth and fifth lumbar or between fifth lumbar and first sacral vertebræ, with herniation into the spinal canal of the nucleus pulposus of the disc, has been increasingly invoked not only as a cause but as *the* cause of all cases of sciatica. Yet others regard lumbar spondylitis or lesions of the sacro-iliac joint as the essential factors. Common to all these hypotheses is the craving of their authors to simplify the problem by invoking a single pathology for all cases, but nature is not interested in simplicity, certainly not in purely verbal simplifications, and the probability is that while acute single-attack cases may be due to an interstitial neuritis, a proportion—as yet unknown—of chronic and recurrent cases may follow upon herniation of an intervertebral disc and the compression of fifth lumbar, first or second sacral roots.

It is virtually impossible to assess the role of lumbar spondylitis, since this condition is very common in middle-aged and elderly men and is often wholly symptom-free, while it is frequently absent in young adults suffering from sciatica. Fibrositis of the lumbo-sacral muscle sheaths is an even vaguer and less satisfactory explanation, but may account for certain cases of pain referred to the distribution of the nerve. In short, it is likely that single-attack cases of very acute onset and relatively brief duration (four to eight weeks) are due to an interstitial sciatic neuritis, but that chronic or recurrent cases occurring in young adults subject to severe physical stresses, and associated in many instances with a history of strain to the lower back, are predominantly due to rupture of an intervertebral disc. In the present state of knowledge no more dogmatic statement can be made.

As has been said, the symptoms and course of an acute sciatic neuritis bear many resemblances to an acute brachial neuritis, though in the latter objective signs (wasting, reflex, and sensory changes) are less common. Injuries to the cervical spine may lead to rupture of a cervical disc, but when this occurs the symptom-complex is rarely that of acute brachial neuritis. Therefore the probability that we have a true interstitial neuritis of the brachial plexus should make us hesitate to reject the notion that a similar process may affect the lumbo-sacral plexus.

Sciatica

The two nerves are affected with approximately equal frequency. The symptoms may develop quite acutely with pain and stiffness in the small of the back, that is, with lumbago, and in a few days pain appears along the course of the sciatic nerve. Another mode of onset is that in which for a variable period of weeks walking or movements tending to stretch the nerve provoke transient accesses of pain along it. Finally, the pain rapidly reaches a climax of intense and disabling severity. When this occurs, any position of the limb in which the nerve is on the stretch becomes acutely painful, the pain radiating from buttock or hip to foot. It is often most intense in the

region of the buttock just mesial to the greater trochanter, near the posterior iliac spine, at the sciatic notch, in the middle of the back of the thigh, behind the knee, and down the lateral aspect of the leg and on the dorsum of the foot. It is paroxysmal with a residual dull aching pain, the paroxysms being burning and lancinating. The patient is usually least uncomfortable when lying down with the leg slightly flexed at hip and knee and rotated out. When standing the leg is kept flexed at these joints, with the heel just off the ground and the pelvis tilted up on the affected side. A compensatory scoliosis offsets this tilting.

Tingling sensations are felt over the cutaneous distribution of the sciatic nerve—that is, over the lateral aspect of the leg and dorsum of the foot. All muscles supplied by the nerve are extremely tender when pressed or stretched, and they become flabby. The calf and plantar muscles are exquisitely painful and may be the seat of recurrent cramps.

The tendon jerks are usually all brisk in the initial acute stage, but in severe and in many chronic cases the ankle jerks may be diminished or abolished, and some wasting and weakness of muscles, more especially of the dorsiflexors, may ensue. Fibrillation in the muscles is not uncommon and may persist for years after recovery. If, with the patient lying on his back, the extended leg be lifted by the heel, great pain is felt as soon as the nerve becomes taut, that is, when the leg has been lifted through about 40° above the horizontal. Pressure over the nerve is also painful.

The severity and duration of the affection vary widely from case to case, and depend largely upon how soon the patient took to his bed after the onset and how long he was kept there. During the first week the pain may be excruciating in severity, but it then progressively abates, and in uncomplicated and adequately treated cases recovery ensues within six to eight weeks. However, some cases become chronic, chiefly those that remained ambulant in the early stage, and the pain persists, with wide fluctuations in frequency and severity, for many months. On the whole, acute attacks of maximal severity are less subject to recurrence than attacks of subacute or insidious development: a fact that may be due to those differences in ætiology already discussed. Certainly subacute attacks may recur at varying intervals for years, with intervals of complete or of incomplete freedom from pain.

The clinical picture and course especially associated with rupture of a lumbar or lumbo-sacral intervertebral disc may be summarised as follows: There is commonly, though not invariably, a history of a strain to the back. The patient is bending to lift a heavy object. This may slip from his grasp, or its weight may suddenly increase if some helper allows it to drop from his grasp. Something is then felt to "give" in the patient's lower back and either an acute "lumbago" follows or he becomes recurrently aware of aching pain and stiffness in this region. Then follows a variable period of what is called "low back pain," and ultimately pain begins to radiate down the back of the thigh and then the lateral aspect of the leg to the ankle. Stooping increases this pain, as also does standing and sometimes sitting on a hard chair. Thereafter the picture is that already described as typical of sciatica. In the early stages nothing may be found other than rigidity of the lumbar spine and the tilting of the pelvis and scoliosis already mentioned. The muscles supplied by the sciatic nerve are commonly tender to pressure, and straight leg raising is painful. Sooner or later the ankle jerk diminishes or is abolished, and there is some subjective numbness along the outer side

of the leg with or without objective impairment of tactile or painful cutaneous sensibility. Some wasting of calf muscles and thinning of the tendo Achillis ultimately ensues, and weakness of dorsiflexion may be present.

Intrathecal air injections (air myelograms) may reveal the presence of some projection into the thecal space.

Diagnosis.—Few familiar conditions are more often erroneously diagnosed upon inadequate grounds than chronic sciatica. Osteoarthritis of the hip is not infrequently so diagnosed. In this there is no noteworthy tenderness of the sciatic nerve or of the muscles supplied by it, and the ankle jerk is never affected, but there is limitation of the range of active and passive movement at the hip. If the heel of the extended leg be struck a smart blow by the observer's palm, there is pain in the region of the hip in arthritis but not in a chronic case of sciatica.

A Symptomatic Sciatica due to pressure upon the nerve or its component roots by a vertebral or intrapelvic growth does not really present a close resemblance to the affection just described. The nerve is never so tender to pressure nor are the muscles, relief from pain is more rapid and complete when the patient is put to bed, and the pain has not the intense burning character of true sciatica. Moreover, in the latter the affection is always unilateral, while in cases of pressure, bilateral signs and symptoms are common. Sooner or later progressive paralysis, wasting, and sensory loss in the distribution of the affected nerve roots make their appearance, together with the clinical indications of the underlying growth.

In every chronic case of what appears to be sciatica, a rectal and a radiological examination should be made.

Treatment.—Rest in bed is an imperative necessity in every case of sciatica, whatever its ætiology, and the prognosis as to duration is always best when this step is taken at once. The patient generally finds his own positions of maximum comfort, and fixation of the limb in the adducted and extended position is rarely tolerated in early and severe cases. The leg should be supported fully by pillows in whatever position it lies. Even in cases where the severity of the pain allows the patient to leave his bed for the closet, he should be discouraged from doing so, and if the use of the bed-pan is, as it may be, extremely painful or objected to, a compromise may be made by the use of a commode in the bedroom. For the first few days the use of morphia may be necessary to secure sleep and to relieve pain, but as soon as possible aspirin with or without codeine ($\frac{1}{8}$ to $\frac{1}{4}$ gr.) and given at regular intervals should be substituted. A barbiturate at night may also be indicated, or a combination of chloral (10 gr.) and sodium bromide (20 gr.). The latter may be given at about seven o'clock in the evening and repeated some three hours later if necessary. In elderly patients it is best to avoid heavier bromide dosage than this. As neither sciatica nor brachial neuritis is primarily an affection of the nervous elements in the nerves or nerve roots concerned, it follows that the employment of vitamin B_1 preparations has no place in treatment. The limb should be kept warm with cotton wool or woollens. The gentle application of a methyl salicylate liniment followed by the application of an ordinary radiant heat lamp may give relief, or an electrically heated pad may be applied. In the acute stage no more active treatment should be given. Massage, movements, or diathermy should be reserved for the convalescent stage or for chronic cases.

The chronic case of sciatica presents one of the most difficult of therapeutic

problems, and many remedies at first hailed as universally successful have had their brief day of apparent triumph and have passed, or are passing, into oblivion. They include stretching the nerve under anæsthetic, injecting it with normal saline solution, injecting the subcutaneous tissues of the thigh with oxygen, turpentine baths, cupping, "ray" treatment and electro-therapy of various forms. More recently epidural sacral injections of a normal saline solution containing novocain have been employed, while spa treatment and all that this implies in baths and mechano-therapy is still with us. In the individual case not one of these can be confidently relied upon to secure relief, but it must be admitted that their frequent failure is often to be attributed to their use *as a substitute* for the only really essential element in treatment, namely, an adequate period of rest in bed. Rest is monotonous, lacks the impressiveness of electro, mechano, and "ray" therapy, and may be economically difficult or impossible, yet an adequate period of rest is not seldom far more economical in the long run than a changing over from one method of active treatment to another. Therefore, the ambulant case of chronic sciatica should be first put back to bed, and while there massage, radiant heat, diathermy, or other chosen method can be given a reasonable opportunity to prove its value. Other modes of treatment call for brief mention. The highly variable procedures known as "manipulation" of the lumbar spine or sacro-iliac joints have their followers, but it is probable that such success as they achieve is in cases wrongly diagnosed as sciatica. A somewhat comparable statement may be made in respect of the intramuscular injection of novocain into painful spots in muscles. Whatever the value of this in conditions unassociated with any form of lesion of the sciatic nerve, it can be no more than a palliative of very limited scope in sciatica.

The suspected case of herniated intervertebral disc should always be given an adequate period of complete rest in the supine position before surgical intervention is considered. It is certain that many cases of this kind do become symptom-free after conservative treatment alone. It is already too common to encounter patients who have been subjected to laminectomy but have never been rested. A final balance of opinion as to the indications for surgical intervention has not yet been reached. Each case must be considered on its merits: the severity of pain, its duration, tendency to recurrence, the nature of the subject's work, and so on. It can be stated, however, that laminectomy for this lesion should be expertly performed if it is not to produce a disability as severe as that it is designed to remedy.

Brachial Neuritis

As in the case of sciatica this is an affection of adults, and may be acute or subacute in onset. Pain first appears at the root of the neck in the region of the plexus, spreading within a few days downwards into the arm and hand. In incidence and character the pain resembles that of acute sciatica, and there are usually localised sites on the lateral aspect of the limb where it is maximal. The patient cannot lie on the affected side and the hanging position of the limb, or its active elevation, is very painful. During the night pain may reach almost intolerable intensity so that the patient has to get up and walk about. Physical examination may reveal little beyond tenderness of muscles, pain on pressure over the brachial plexus and upon stretching it. The arm jerks

are usually brisk, and wasting, weakness, and objective sensory loss are exceptional.

When adequately treated from the outset, the intense pain dies down in a week or so and recovery is complete in from six to eight weeks.

The brachial neuritis that may follow the injection of foreign proteins (tetanus antitoxin, diphtheria, antitoxin, T.A.B., etc.) is a more serious affair, though fortunately a rare one. Within from a few days to about two weeks after the injection, and with or without the usual manifestations of "serum sickness," pain develops in the neck, shoulders, and chest. Weakness comes on rapidly in muscles supplied by the upper roots of the plexus, though all muscles in the limb are liable to involvement. The condition is usually bilateral, though not bilaterally symmetrical. Deltoid, serratus anterior, the rhomboids, the spinati, and triceps are the muscles most often affected. Wasting soon appears and the disability may be severe. Pain persists for a varying period, sometimes for several weeks. The tendon jerks vary according to the incidence of the paralysis, and one or more of them may be abolished. Sensory loss is minimal and may be absent. There may be an associated paralysis of one or more cranial nerves. Recovery slowly sets in, but is not always complete in all the affected muscles. This variety of brachial neuritis has also been recorded quite apart from protein injections, and it has been suggested that these play no causative role when brachial neuritis follows them, but that the association is always coincidental will not readily be accepted by those who have seen it.

Treatment.—The same general principles of rest, medication, and local treatment as have been mentioned in the case of sciatica apply here. In severe cases it is best to put the patient to bed at once and to rest the affected arm in the most comfortable position on pillows. Its use should be wholly avoided until recovery is manifestly under way. The necessary immobilisation of the limb is apt to lead to some fixation of the shoulder joint, and to avoid this the arm should be carefully moved by the nurse for a few moments morning and evening so as to keep this joint mobile. When this measure is neglected it is not rarely found after recovery that there is partial ankylosis of the shoulder.

In the paralytic form associated with serum injections the principles governing the treatment of the paralysis of poliomyelitis apply.

NEUROMA

The nerves may be the seat of tumours which are known as neuromata. In the *true neuroma*, or ganglioneuroma, nerve fibres and ganglion cells form part of the structure of the tumour. This rare form of neuroma is found only in connection with the sympathetic nervous system in the thoracic or abdominal cavities. The *false neuroma*, or neurofibroma, is not uncommon. It arises in the connective tissue of the nerve and may be central, separating the nerve fibre bundles or situated at the side of the nerve trunk. It may be the seat of cystic or myxomatous degeneration. Neurofibromata may be single or multiple, and in the latter case the tumours may be confined to a single nerve or nerve plexus, or be widely diffused. In size they vary from tiny nodules to large masses of several inches diameter. They are congenital, of unknown origin, and may be found in epileptic or mentally defective subjects.

It is the solitary neurofibroma which is usually responsible for symptoms, and these consist in pain along the course of the nerve, and also, though rarely, in objective sensory and motor symptoms. In *multiple neurofibromatosis* innumerable tumours of soft consistence stud all the peripheral nerves. Occurring on cranial or spinal nerve roots they may produce compression symptoms. Neurofibrom on the auditory nerve forms the so-called acoustic tumour, or tumour of the ponto-cerebellar angle.

When multiple neurofibromatosis is associated with cutaneous pigmentation and the presence of multiple, sessile, and pedunculated tumours on the skin, the condition is known as "von Recklinghausen's disease" or "Molluscum fibrosum."

Tubercula dolorosa is the name given to collections of tiny neurofibromata situated on the terminal twigs of cutaneous nerves, and giving rise to considerable tenderness and pain.

All these forms of tumours on nerves tend to be progressive, but do not call for treatment unless pain, or, in the case of tumours within the skull and vertebral canal, signs of compression of adjacent structures occur. In these circumstances the offending tumour should be removed when possible.

AFFECTIONS OF THE SPINAL NERVES

General Observations on Peripheral Nerve Lesions

The symptoms of a peripheral nerve lesion may be of one of the following four types: (i) complete interruption; (ii) compression with partial interruption; (iii) partial interruption with signs of irritation; and (iv) partial interruption with signs of regeneration.

The majority of cases of isolated affection of one or more peripheral nerves are traumatic in origin, at least in those cases where there is severe interference with conduction, and partial interruption is on the whole more common than complete interruption. The following clinical criteria are of value in differentiating the four syndromes given above.

In Complete Interruption there is total paralysis of all muscles exclusively supplied by the nerve. These muscles waste rapidly and profoundly, and, for a period of some weeks beginning from about the third week after interruption has occurred, show the reaction of degeneration. The essential elements of this reaction are a loss of faradic excitability and increased and altered galvanic excitability. The threshold of effective stimulation by the continuous current may be lowered, and the resulting contraction is slowed and tends to pass as a wave down the stimulated muscle from one electrode to the other. The polar alteration so commonly described as part of the reaction of degeneration is an inconstant and unimportant thing. The significance of this reaction is that the muscle which shows it is completely denervated for the time being. Such a muscle when tapped with a percussion hammer responds by the same slow, wave-like type of contraction as is seen on using the galvanic or continuous current, and by careful tapping in this way as much information may be obtained as by electrical testing, and with considerably less difficulty.

The paralysed and wasted muscles are painless to pressure, tactile sensibility being lost over a wider area than is pain sense. The area of sensory change is maximal for the nerve affected. Pressure on the nerve below the

level of the lesion does not produce a tingling sensation in its cutaneous distribution.

In Compression with Partial Interruption.—The muscles supplied by the nerve may not be completely paralysed though they generally show some wasting. They are usually very tender on pressure or on stretching. This is especially the case with muscles supplied by the medial popliteal division of the sciatic nerve and those supplied by the median nerve. In minimal lesions of the nerve this tenderness may be more prominent than weakness, and may constitute a graver disability on account of the pain produced by voluntary contraction. As in complete interruption the tendon jerk of any muscle affected is usually lost. The electrical reactions may show no qualitative alteration. The area of sensory change may be less than the complete distribution of the nerve concerned. There is usually a small area of total pain and temperature loss surrounded by a larger area of complete tactile loss, within which there is qualitatively altered sensation to pain and temperature. Pinprick is peculiarly painful and diffuse in the sensation it evokes within this area.

Partial Interruption with Signs of Irritation.—This syndrome is always the result of partial division by a wound or of the involvement of an intact nerve trunk in cicatricial tissue from an adjacent wound. The greatest degree of irritation is seen in median and medial popliteal nerve lesions. The irritation varies in degree from slight pain and cutaneous hyperæsthesia with muscle tenderness to excruciating burning pain in the affected region and severe trophic lesions. The signs of interruption of conduction may be trivial. The most severe type is that associated with *causalgia*, a form of pain which may be of intense severity, and when long lasting reduces the sufferer to a pitiable state. The pain is aggravated by any movement of the part, active or passive, or by a jarring of the bed on which the patient lies; the pain is mainly superficial. This clinical picture is commonly the result of gunshot wounds which have just glanced the nerve without severing any or many fibres. Motor signs of irritation are contracture and fibrous infiltration of muscles, muscular spasms and, rarely, actual hypertrophy of muscle.

Signs of Regeneration are both motor and sensory. On the motor side the pilomotor muscles in the affected cutaneous area regain function and the limb muscles regain tone before voluntary power returns. On the sensory side percussion of the nerve below the lesion elicits a tingling sensation within the skin area which is the seat of sensory loss. All forms of cutaneous sensibility begin to return together, first at the proximal end of the anæsthetic area, but sensations elicited by stimuli here are referred to the distal end of the anæsthetic area (" peripheral reference "). Gradually the area of sensory change lessens in size, beginning to recede at the proximal end. Thermal and painful sensations are apt to be intensified and to be badly localised.

The electrical reactions also begin to return to normal, and trophic lesions to clear up.

LESIONS OF THE BRACHIAL PLEXUS AND OF NERVES DERIVED FROM IT

The brachial plexus is derived from the lower four cervical and the first thoracic spinal nerve roots. These roots are purely morphological in the

arrangement of their nerve fibres, whereas the nerve trunks issuing from the plexus distally are physiologically arranged, flexor muscles being supplied by one nerve, extensors by another. The function of the plexus is to effect this rearrangement, and it follows that the topography of the sensory and motor paralyses in plexus lesions will depend upon the situation of the lesion. There are thus three possible types of plexus lesion: radicular lesions involving the roots entering into the plexus, plexus lesions involving the trunks and cords, and distal lesions which correspond to combined lesions of the peripheral nerves.

Radicular Lesions form the majority of cases, and fall into two groups: (i) upper plexus type, in which the fifth and sixth cervical roots are concerned; and (ii) lower plexus type, in which the eighth cervical and first thoracic roots are concerned. (i) The muscles supplied by the fifth and sixth roots and affected in lesions of these roots are the deltoid, biceps, brachialis anticus, supinator longus (brachio-radialis), supra- and infra-spinatus, serratus magnus (S. anterior), rhomboids, clavicular part of pectoralis major and subscapularis. The sensory loss involves the outer aspect of the shoulder and upper limb; biceps and supinator jerks may be lost. (ii) The eighth cervical and first thoracic roots supply the flexor muscles in the forearm and the small hand muscles. The sensory change includes the ulnar aspect of forearm and hand. There may be an associated cervical sympathetic paralysis in first thoracic root lesions. Lesions of the trunks and cords of the plexus are not so common as those of the roots or of the upper trunk formed by the junction of the fifth and sixth cervical roots. Occasionally, also, in gunshot and stab wounds the posterior cord of the plexus may be injured, giving rise to sensory and motor symptoms in the distribution of the circumflex and musculospiral (radial) nerves.

Ætiology of Brachial Plexus Lesions.—The majority of plexus lesions are traumatic in origin and arise from the violent forcing of the shoulder and arm into abnormal positions. Thus traction on the arm falls on the shoulder, or pressure exerted on the shoulder from above may tear the upper plexus roots either at their points of attachment to the cord or in the intervertebral foramina. In forced adduction of the shoulder the clavicle may be forced backwards, and may compress the plexus against the first rib. The familiar type of birth palsy involves the fifth and sixth roots or the trunk formed by their union, and results from force exerted on the arm when this does not present normally.

Upper plexus lesions form the majority of cases, and the lower plexus type is relatively uncommon, except when associated with a lesion of the upper plexus.

Apart from trauma, the nerve roots entering into the plexus may be involved within the meninges by tumours or by syphilitic or tuberculous inflammatory processes; within the vertebral foramina by arthritic changes, by tuberculous caries, or by new growth; in the neck by new growth or by gunshot or stab wounds. The production of plexus injury by cervical or first thoracic ribs is dealt with below.

Symptomatology.—In upper plexus lesions there is both weakness and wasting of the affected muscles, deltoid and biceps being usually the most severely affected and showing a reaction of degeneration. The arm hangs adducted with the forearm pronated. It cannot be abducted nor can the elbow be flexed. The extent and degree of sensory loss is very variable. In

slight injuries one or more of the muscles innervated by the damaged roots may escape. In lower plexus lesions there is weakness and wasting of the hand muscles, and oculo-pupillary (cervical sympathetic) symptoms when the first thoracic root is injured near its point of origin from the cord.

Treatment.—The processes of repair which follow severe injuries to the plexus and include fibrosis and matting of the nerve trunks render surgical treatment out of the question in all but exceptional cases. The treatment of paralysed muscles must be carried out on the lines laid down in the section dealing with Acute Poliomyelitis (*vide* p. 628), and pain when present may be treated by radiant heat and suitable drugs.

Obstetric Paralyses of the Brachial Plexus.—As has been mentioned, these are more commonly of upper than of lower plexus type. They usually arise in head presentations when the shoulder is delayed or the arm extended, and when these structures are manipulated or pulled upon. Traction on the arm or forcible lateral flexion of the neck may tear the roots either at their attachment to the cord or in the intervertebral foramina. In a typical birth palsy the muscles paralysed are deltoid, biceps, brachialis anticus supinator longus and brevis (brachio-radialis and supinator), and infraspinatus. The humerus is rotated inwards, the forearm extended, and the hand pronated. Usually there are no sensory phenomena. Less commonly a lower plexus paralysis with signs of cervical sympathetic involvement occurs. Associated complications may be fractured clavicle and humerus, dislocation of the shoulder, and hæmorrhage into the sternomastoid.

Prognosis.—Unless recovery takes place rapidly and becomes complete within a few weeks, improvement is likely to be slow and recovery incomplete.

Treatment.—The arm should be fixed in an abduction splint in severe cases for a short time, and subsequently the use of the arm should be encouraged by bandaging the normal arm to the side for short periods. Massage may be of some value. The slight cases recover without treatment.

Rib Pressure Syndromes

Certain anatomical variations occur in the segmental derivation of the brachial plexus. Thus the plexus may receive a large quota of fibres from the fourth cervical root and an unduly small one or none from the first thoracic root. Such a plexus is said to be prefixed. On the other hand, less commonly, the fifth cervical quota is small and a large quota from the second thoracic root is present. Such a plexus is said to be post-fixed. The development of the costal elements of the vertebræ follows that of the plexus, so that with a prefixed plexus a supernumerary rib may develop from the seventh cervical vertebra, while a post-fixed plexus may interfere with the development of the normal first thoracic rib, which then retains a rudimentary form. When the adjustment between plexus and ribs is perfect, no abnormal pressure is exerted on the roots, but when the development of the costal process is in excess of the plexus alteration, the lowest nerve root in the plexus may be stretched over the costal element, and symptoms of neuritis and damage arise. Thus a cervical rib may stretch the seventh and eighth cervical roots, or a rudimentary first thoracic rib may similarly affect the first thoracic root. The following types of rudimentary rib occur: (i) an exaggerated costal process of the seventh cervical vertebra which is prolonged forwards and downwards as a fibrous band, to be attached to the first rib; (ii) a short rib

articulated at its origin and continued as above; (iii) a long jointed cervical rib attached by a fibrous band to the normal first rib; (iv) a cervical rib articulated at each end, anteriorly with the first rib; (v) a rudimentary first thoracic rib attached to the sternum by a fibrous band. The first and last of these forms are not readily visible in a radiogram, but may yet be responsible for plexus pressure.

Whether the injury to the nerve root is caused by the bony or the fibrous part of the rib depends upon the length of the former.

An abnormal costal element is rarely the sole anatomical anomaly present, but is frequently associated with cervico-dorsal scoliosis and developmental abnormalities in the vertebræ in this region. As a consequence of all these anatomical factors, the upper thoracic outlet is asymmetrical, being higher and narrower on the side on which pressure symptoms arise.

Ætiology.—Given the anatomical anomalies enumerated, certain other factors enter into the causation of symptoms. These include compression of nerve trunks and of subclavian artery between clavicle and rib, the two forming the arms of a vice which tends to close when the arm is elevated or retracted: further, the rhythmical movements of the thorax in respiration tend to aggravate any nerve root stretching or compression that may be present, and finally, there may be pathological reactions, such as the formation of fibrous tissue tying down nerve trunk and artery to the abnormal rib.

The element of costo-clavicular compression may, by repeatedly inflicting minor damage on the subclavian artery in its third part, lead to aneurysmal dilatation of the artery, and this may be followed by clot formation and partial occlusion of the vessel, and in some instances by embolism, tiny fragments of clot becoming impacted in digital arteries where they produce small infarcts or gangrene. These last complications are rare.

Added to these anatomical and pathological factors, there is also to be taken into account a drooping of the shoulder girdles that occurs in fatigued or debilitated persons, on the whole more commonly in women. This last factor may lead to the development of pressure symptoms hitherto absent.

The importance of the drooping shoulder girdle is illustrated by the not rare occurrence of minor plexus or vascular compression symptoms in persons with no abnormality of the upper costal outlet. Cases of this order are those formerly described as the *scalenus anticus syndrome*. This muscle does not play a primary or constant part in the appearance of pressure symptoms with a normal costal and thoracic structure, but a drooping girdle allows nerve trunk and artery to become stretched over a normal first rib.

Symptomatology.—This may be entirely or largely subjective, or there may be muscular atrophy, sensory loss, and vasomotor changes in the limb. The initial symptoms are pain and paræsthesiæ. Both symptoms tend to be maximal in the hand, but vary greatly in distribution and intensity from case to case. Usually the pain radiates down the forearm into the hand and digits; it is aggravated by anything which depresses the shoulder girdle, such as carrying a parcel or wearing a heavy coat, and is relieved by elevating the shoulder girdle. It may come on with great intensity while the patient is in bed. These subjective symptoms may persist for many months without the development of any objective motor or sensory changes. When muscular wasting appears, it conforms to one of two types; a median type with a selective incidence of wasting in abductor pollicis brevis and opponens pollicis alone. The thenar eminence then is flattened in its radial half, the shaft of

the metacarpal bone becomes subcutaneous, while the other thenar muscles escape. This type of wasting is pathognomonic of cervical rib pressure. The other type of muscular atrophy corresponds to an ulnar distribution, the wasted muscles being the interossei, and the hand tends to assume the *main en griffe* posture. Sensory changes are variable and inconstant; they may be on the radial or the ulnar side of the arm, the former in thenar atrophy and the latter in the ulnar type. There is a clinical type in which vasomotor symptoms predominate. These consist of redness, cyanosis or œdema of the hand, with subjective sensations of heat or cold. The radial pulse may be smaller than on the normal side in those rare cases where the subclavian artery is raised over the rib. In rare cases of this kind blood clot may form in the subclavian artery, and embolism occur distally, blocking the artery in the arm at its bifurcation at the elbow, or one of its distal branches. In these circumstances gangrene may develop in one or more finger tips. When this happens it is likely to be in a case which presents no signs of nerve pressure.

Diagnosis.—The presence of long-continued pain and paræsthesiæ in one arm, especially in a woman, when associated with vasomotor changes, should lead to a suspicion of cervical rib and to an X-ray examination of the neck. Muscular atrophy may be considerably delayed in many cases, and appear only after long months of pain. A history of factors which relieve or aggravate pain is of importance for the reasons given above. When atrophy is present the condition has to be differentiated from progressive muscular atrophy and lesions of the lower part of the cervical enlargement of the cord. In these the small hand muscle wasting is global, and rarely selective as in the thenar type of wasting described. Moreover, some degree of involvement of the other hand develops sooner or later in both these conditions.

Diagnosis presents greatest difficulties when radiograms yield no definite information, as may be the case with a fibrous "rib," and no objective motor or sensory symptoms are present. In these circumstances a careful history will generally suffice to distinguish rib pressure from brachial neuritis.

Treatment.—When there is no muscular atrophy and pain is the prominent symptom, complete relief may be obtained by measures which tend to raise the normal level of the shoulder girdle. At first the arm may be carried in a sling, and then massage and remedial exercises designed to increase the tone and power in the girdle muscles should be carried out. General tonic treatment and careful attention to the patient's nutrition and amount of exercise are important. Pain may be relieved by the use of aspirin, phenacetin, and allied drugs.

When muscular atrophy is present it is doubtful if any treatment short of surgical removal of the abnormal rib, thoracic or cervical, is adequate, and in some cases where pain persists in spite of the measures described above, resection may be necessary.

The Phrenic Nerve.—Paralysis of this nerve is uncommon, but when present may be due to lesions of its cells of origin in the third, fourth, and fifth cervical segments of the cord (poliomyelitis, motor neurone disease, compression); to lesions of its roots (vertebral disease, meningitis) or to lesions of the nerve in neck or thorax, where it is occasionally involved in new growths or inflammatory processes. The symptom is paralysis of the diaphragm. When unilateral this may be difficult to detect apart from radioscopic screening; when bilateral there is slight dyspnœa on exertion, and bulging of the abdominal wall on inspiration.

When associated with paralysis of other respiratory muscles the danger of death from asphyxia is considerable unless some function is rapidly restored.

The Circumflex Nerve.—The nerve may be damaged in injuries to the shoulder, or be affected by a toxic parenchymatous neuritis. The symptom is paralysis of the deltoid, with or without sensory loss in the skin covering the lateral aspect of this muscle. In complete lesions the deltoid wastes rapidly and profoundly, and recovery is generally delayed and imperfect. The arm cannot be abducted, and forward and backward movements of the arm are weakened. Arthritic changes in the shoulder joint may occur in permanent paralysis of the muscle.

The Long Thoracic Nerve (nerve to serratus anterior).—This nerve innervates serratus magnus. It may be damaged in injuries to the shoulder region by excessive strain, as in carrying weights or in keeping the arm elevated and outstretched unduly.

It is not infrequently affected alone by toxic processes (after diphtheria, typhoid, influenza, and other infections). There is often some associated paralysis of the middle or lower part of trapezius. The normal function of the serratus magnus is to draw the scapula upward, forward, and outward, and to advance the point of the shoulder. When paralysed, elevation of the arm is slightly weakened, and when the arm is advanced to the horizontal, the vertebral (medial) border of the scapula stands out from the thorax and is said to be "winged."

The Musculospiral (Radial) Nerve.—Owing to its long and exposed course this is the most frequently injured branch of the brachial plexus. The majority of lesions are traumatic, the nerve being damaged as it passes round the outer side of the arm. Simple compression is the commonest form of injury, the arm being pressed against something hard, or compressed by a tourniquet. It is rare for the nerve of a perfectly healthy subject to sustain damage in this way, the majority of the patients being chronic alcoholics whose peripheral nerves are already poisoned. Other predisposing factors are debility, chronic plumbism, and recent infections such as typhoid. Other forms of injury are the involvement of the nerve in fracture of the shaft of the humerus, and pressure on the nerve in the axilla by a crutch.

Symptomatology.—This varies according to whether the nerve is damaged distal to the offset of the branch to the triceps or not. In the former case triceps and anconeus escape, and the supinators, extensors of the hand and of the fingers, and the extensors and long abductor of the thumb are paralysed. There is wrist-drop, and the wrist and digits cannot be extended, except that the interossei maintain extension of the distal and middle phalanges. The grasp is weakened owing to the flexion at the wrist which accompanies it, and which is due to loss of the synergic fixation of the wrist that is part of the complete movement of grasping. Supination of the forearm is lost, except when the biceps is contracting and the elbow flexing. In crutch paralysis the triceps is involved also. Sensory loss is inconstant, but when present occurs over the radial half of the dorsum of the hand and over the proximal segments of the thumb, index, and middle fingers.

Prognosis and Treatment.—Recovery is the rule except in severe crushing of the nerve in association with fracture. Slight pressure palsy recovers rapidly without special treatment, but in severer cases where the muscles show a reaction of degeneration, recovery is delayed. The essential part of treatment is the placing of the paralysed muscles in the position of physio-

logical rest—that is, moderately shortened. This is done by the use of an anterior forearm and hand splint, which keeps the wrist and digits slightly extended. Active exerises should be carried out daily, care being taken to prevent full extension of the paretic muscles.

The Median Nerve.—Isolated paralysis of the median nerve is not common, and is generally traumatic in origin. It may be affected with other nerves in compression of the limb. Slight median nerve paralysis associated with interstitial neuritis is sometimes found in hand workers (joiners, locksmiths, ironers, etc.). Toxic parenchymatous neuritis of the nerve occasionally occurs in association with various infections.

Symptomatology.—When the nerve is damaged in the upper arm the following muscles are affected: flexor carpi radialis, flexor sublimis, and part of flexor profundus digitorum, the pronators, flexor longus pollicis, opponens pollicis, abductor brevis pollicis and flexor brevis pollicis, and the lateral two lumbrical muscles. The full extent of sensory change includes the palm of the hand radial to a line drawn along the long axis of the limb down the middle of the ring finger, and also the palmar aspect of the digits and thumb. On the dorsum it includes the distal portions of the same digits. In incomplete lesions a less extensive area of altered sensibility may be present. In addition to these objective motor and sensory phenomena, in incomplete lesions of the nerve there may be marked tenderness of the paretic muscles, severe pain in the distribution of the nerve, the so-called causalgia, and trophic changes in the skin and nails of the affected area. Thus the nails may be rounded and furrowed and the skin shiny and atrophic.

Prognosis and Treatment.—The prospect of recovery in severe lesions is by no means so good as in the case of the musculospiral nerve. In traumatic lesions resection and resuture may be called for.

The Ulnar Nerve.—This nerve is more commonly injured than the median. Isolated lesions are generally traumatic. The nerve may be crushed in fractures of the internal condyle (medial epicondyle) of the humerus, or may become later involved in callus formation after such a fracture. The paralysis of the nerve in the latter case is gradual and may be long delayed. The nerve may be exposed to repeated minor injuries, as it lies behind the condyle, and develop a neuritis with paralytic symptoms. An isolated toxic neuritis of the nerve occasionally follows some infection.

Symptomatology.—Ulnar nerve paralysis is peculiarly disabling to the hand owing to the paralysis of the interossei. The thumb cannot be adducted and the little finger is almost immobilised. The fingers cannot be flexed at the metacarpophalangeal joints or extended at the distal joints, though in this respect the index and ring fingers are less disabled than the remaining digits. Gradually the "claw hand" is produced by the overaction of opponents of the interossei; the fingers are hyperextended at the proximal and flexed at the distal joints. The hypothenar eminence and the mesial part of the thenar eminence disappear.

LESIONS OF THE LUMBAR AND SACRAL PLEXUSES

The lumbar and sacral plexuses and the peripheral nerves of the lower limbs are much less frequently affected than the plexus and nerves of the upper limb. Isolated paralyses of anterior crural (femoral) or

obturator nerves are rare, and while the sciatic nerve is more frequently the seat of disease, it is rarely completely paralysed apart from gunshot wounds.

The Sciatic Nerve.—The nerve trunk, or the roots which enter into its formation, may be involved by tumours of the sacrum or in the pelvis, or by a syphilitic radiculitis. The nerve is commonly the seat of an interstitial neuritis which is the pathological process responsible for sciatica, a condition which has already been described (*vide* p. 703).

In damage to the nerve from pelvic lesions, tumours or compression exerted by the fœtal head in pregnant women, it is the peroneal division of the nerve which bears the brunt of the damage. The symptoms of a lesion of the peroneal (lateral popliteal) division in this situation are : paralysis or paresis of the dorsiflexors of the foot and toes, of the peronei, with sensory loss over the outer aspect of the leg and over the dorsum of the foot. The foot hangs down in the equinovarus position and cannot be dorsiflexed or everted. Secondary shortening of the calf muscles may render the foot-drop a permanent disability.

The Lateral Popliteal Nerve.—Emphasis should be laid upon the isolated affection of this nerve since it is not uncommon. It may occur in otherwise healthy adults quite apart from discoverable local injury. In these circumstances its ætiology is unknown. Its appearance is often preceded by pain along the outer side of the leg. After this has been present for two or three days a sudden paralysis, usually severe in degree, of all the muscles supplied by the nerve is seen. The foot hangs loosely down in the position of equinovarus. The patient can stand on tiptoe, but he cannot dorsiflex the foot and he cannot run. There is sensory loss of varying degree over the outer aspect of the leg and on the dorsum of the foot to the base of the toes. After some weeks a degree of wasting of the affected muscles makes its appearance, but is rarely profound. Recovery is very slow and frequently incomplete. Among the special circumstances in which this nerve may be paralysed are compression of the nerve trunk by a garter or a bandage round the upper end of the fibula where the nerve winds round the bone. In diabetes, and occasionally in typhoid, this nerve may be the seat of a neuritis. Treatment consists in the wearing of a foot-drop support by day and of a night shoe when in bed, so that the foot is constantly kept at right angles to the line of the leg.

The Tibial or Medial Popliteal Nerve.—Apart from gunshot wounds and comparable injuries, isolated paralysis of this division of the sciatic nerve is uncommon. In complete lesions the symptoms are paralysis of the calf and plantar muscles and sensory loss over the sole of the foot and the posterior aspect of the leg in its lower half. The atrophy of the plantar muscles renders the sole hollow, the proximal segment of the toes is hyperextended and the terminal segments flexed. Perforating plantar ulcers may develop when sensory loss is complete.

The Anterior Crural (Femoral) Nerve.—Paralysis of this nerve is very rare, and when it occurs is the result of pelvic injuries. The symptoms are paralysis of ilio-psoas, pectineus, sartorius, and quadriceps. There is loss of the knee jerk and weakness of extension of the knee. There may be sensory change on the anterior and medial aspects of the thigh. An uncommon malady is an interstitial neuritis of the lateral cutaneous nerve of the thigh, known as " meralgia paræsthetica." It occurs in males, and its symptoms are

pains, paræsthesiæ, and slight objective changes in sensibility in the territory of this nerve on the front and lateral aspect of the thigh. The symptoms are brought on by standing or walking.

OCCUPATIONAL CRAMPS

Under this heading is included a group of disabilities in which the characteristic symptoms are provoked by the effort to carry out some habitually performed muscular action, commonly an action by which the subject earns his livelihood. It follows that the disability appears in the muscles which perform this action, and ends by preventing its accomplishment. The two essential symptoms are spasm and cramp-like pain in the affected muscles. Those who carry out repetitive movements with the right hand and arm are the subjects of the malady, such as clerks, telegraphists, hammermen, and sempstresses. Hence we speak of writer's cramp, telegraphist's cramp, and so on. At its onset an occupation cramp of this type appears only when the specific action is being carried out with a given group of muscles, but in severe and long-standing cases other co-ordinated movements performed by these muscles also come to be impeded in execution. Perhaps the commonest clinical type is writer's cramp, and what is to be said of its ætiology, prognosis, and treatment applies to other varieties of "cramp."

Writer's Cramp.—*Ætiology.*—Hitherto males have formed the majority of the patients, but with the entry of women into clerical occupations it is possible that this statement may have to be modified in due course. The patients are clerks in the third, fourth, or fifth decades of life. In writing there are two motor components, pen-holding and pen-moving. Faulty habits of pen-moving are probably important factors in the production of writer's cramp, and it is this aspect of the act of writing which is predominantly affected. Those who perform the movements of the pen wholly with the thumb and index fingers, or from the wrist downwards, employing the arm as a whole, little, or not at all, are throwing the greatest strain upon a small group of muscles, and appear to be specially liable to this form of occupation cramp. Shorthand writers are said to be immune from this disability.

Symptoms.—The onset is gradual. After a spell of writing the subject finds the pen getting slightly out of control and causing slight disfigurations of his handwriting. He notices that he is grasping the pen with undue firmness, and that the hand readily tires and aches. The thumb and index gradually tend to go into flexion spasm and to slip up the pen, and he cannot freely extend these digits to move the pen up and down the paper. The writing becomes jerky and heavy from the force with which the pen is pressed upon the paper. Gradually the forearm muscles are invaded by spasm, and in course of time the writing of a few words brings the hand to a stop with the pen tightly grasped in the flexed thumb and index. At first all other hand and finger movements are performed with normal freedom, but gradually these also tend to become difficult and painful. In some patients pain is prominent from the outset and may remain the predominant symptoms throughout, cramp being minimal.

Different methods of holding the pen give transient relief, but finally

all devices of this kind fail and the patient becomes unable to write at all. Even the left hand may be invaded if the subject learns to write left-handed.

Course.—The symptoms increase progressively until the attempt to write is finally abandoned and the hand is rested for a prolonged period. Usually recurrence attends the subsequent resumption of writing, but not invariably.

Diagnosis.—Although the symptoms of writer's cramp are extremely characteristic, numerous pitfalls beset the early diagnosis of the condition. Any slowly progressive lesion involving the central nervous mechanism of movement tends to affect finely co-ordinated purposive movements before coarser or simpler movements are impaired or before there is obvious paresis. Therefore difficulty in writing may be simply the expression of such a slowly developing disorder of movement. Paralysis agitans is an example of such an insidiously developing malady which may interfere with freedom of writing before other disabilities are complained of, and this is especially apt to be the case in a professional writer. Other comparable organic diseases will come readily to mind in this connection, and the presence of these should be excluded by thorough investigation before a diagnosis of writer's cramp is accepted. Again, any peripheral nerve affection or joint affection which gives rise to pain on movement of the hand or arm may impair the freedom and comfort of writing. Finally, any painful affection of the tissues of the hand should be excluded.

Treatment.—Although writer's cramp is in all probability primarily due to defective methods of writing, the malady develops at a time when re-education in the act cannot be carried out. Rest is the first essential of treatment, and should be for not less than six months, even in the slightest cases. In the absence of such rest no improvement can be expected. The value of local treatment, such as massage or electrical stimulation, is uncertain. Their use encourages the patient, and their withholding may lead him to feel that nothing is being done for him. Mild galvanism and gentle massage with active exercises are the best forms of local treatment to allow in these circumstances.

If the patient resume writing, the use of a broad-pointed nib and of a thick penholder is advisable.

In violin and piano players, neuralgic or painful forms of occupation neurosis are more common than muscular spasm, but some spasm in the fingers may be present. Treatment must be carried out on the lines indicated above.

THE TICS

A tic has been defined as "a co-ordinated purposive act, provoked in the first instance by some external cause or by an idea; repetition leads to its becoming habitual, and finally to its involuntary reproduction without cause and for no purpose." There are psychical and motor components in a tic. The motor component may consist of sudden jerky co-ordinated movements endlessly repeated. This form is most common in children, and tends to involve the facial, laryngeal, pharyngeal, and upper limb muscles predominantly. This is the so-called simple tic. More complicated reactions may occur consisting in the repetition of some complex act. A special variety of motor disorder allied to the tics is spasmodic torticollis.

In a few cases there is no obvious motor component, but the patient is swayed by imperative ideas and is subject to periodical explosive utterances.

All forms occur in mentally unstable individuals, in whom other neuropathic symptoms may be present.

Simple Tic : Habit Spasm.—This is a malady of highly strung children during the second five years of life. Its onset may be precipitated by ill-health or debilitating factors. The facial muscles are commonly affected, and the child blinks, wrinkles its forehead, or makes any of a series of jerky grimaces. The arms may also be the seat of similar jerky movements. The disorder is increased by anxiety or emotion of any kind, can be controlled momentarily, and ceases during sleep. When the laryngeal musculature is affected the child may make repeated clicking or other sounds. The malady may persist for many months, and even for years. It is often associated with nail-biting, difficulties in feeding, and restless and disturbed sleep. Usually the symptoms clear up entirely, but recurrent attacks are not uncommon.

Diagnosis.—The disease with which simple tic is most likely to be confused is Sydenham's chorea. In chorea the movements are not repetitive, they lead to dropping of objects held in the affected hand, and to defects of articulation. The hand-grasp of the patient with chorea is irregularly sustained. The opposites of all these features obtain in simple tic.

Convulsive Tic.—In this relatively uncommon form the movements have the same character as those of simple tic but are much more violent and widespread, involving sometimes the whole musculature. Complicated and grotesque gestures may occur in periodical outbursts, and the patient commonly presents marked mental instability.

Psychical Tic.—In this form, although there is no muscular spasm in the strict sense of the word, the malady does find motor expression in repeated explosive utterances, which may consist of words, phrases, or sentences. The repetition of words heard in this way is spoken of as echolalia, while if the utterances be obscene we speak of coprolalia. Anxiety neurosis symptoms may be added to this picture, and definite psychotic symptoms may ultimately develop.

Treatment.—The child's general health must first receive attention, and any adverse factors in its home and school environment, psychological or physical, be corrected. The constant reprimands to which many such children are subjected by over-anxious parents are detrimental to recovery. Perhaps the most essential element in successful treatment is the wise management of the child both at work and play. It not infrequently happens that the patients are the children of unstable parents who are ill fitted to assist treatment in the required directions. Firm but kindly discipline, carefully graded physical exercises, a nourishing dietary and, in the matter of drugs, the use of moderate doses of bromide will suffice to effect cure in the majority of cases. Similar considerations should guide treatment in the case of convulsive and psychical tics, but with these the prognosis is invariably bad.

Spasmodic Torticollis.—In this condition there is irregular tonic and clonic spasm of the muscles which rotate the head. Sometimes the extensors of the neck are also involved. As a result the head is periodically forced into abnormal positions. The condition is momentarily under control, but considerable mental effort may be needed to restrain the spasm for more than a few seconds.

Etiology.—It is a malady of adult life, and may occur in persons of any age from the later years of the third decade onwards. The sexes are equally affected. Commonly it arises without any precipitating factor which is discoverable, but pain from cervical spondylitis or fibrositis in the neck muscles may be the exciting factor in a predisposed person. Anxiety and worry are other exciting factors. Most of the patients are highly strung, emotional individuals with a neuropathic inheritance. Recently the view has been put forward that the spasm is the expression of a small lesion of the corpus striatum, but there is no evidence in favour of such an hypothesis. It must be remembered that the carriage of the head in the erect position is a very complex and recently evolved function, and one, therefore, which may easily be disordered from a variety of causes other than focal disease in the brain.

Symptomatology.—The onset is usually very gradual, the patient becoming slowly aware of a tendency of his head to turn to one side. At first he can control this, but with lapse of attention, and particularly under any kind of stress, the movement gains in frequency and force. The neck muscles are bilaterally involved, but on simple inspection the muscle most obviously in spasm is sternomastoid. The crossed trapezius is usually affected simultaneously, and as the malady progresses other muscles enter into spasm. With powerful action of the neck extensors the head may be retracted (retrocollic spasm), and associated with this is overaction of the frontales and elevation of the eyebrows. This is a normal association when the head is thrown back voluntarily, and its presence here indicates that we are dealing not with simple muscular spasm but with a more complex phenomenon, namely, a movement involving normally co-operating muscles, and probably initiated from a high cerebral level. The spasm may be almost wholly tonic, or clonic exacerbations may be superimposed upon it, and the predominantly tonic form cannot be differentiated in respect of ætiology or causation from the clonic variety. In severe cases cramp-like pain usually accompanies the spasm, and the latter may be so forceful as to require considerable effort to overcmoe it passively. Hypertrophy of the sternomastoid is sometimes seen in long-standing cases. It is said that deviation of the head to the left is more common than to the right.

Prognosis and Treatment.—Massage, active exercises against resistance, and general rest will sometimes effect a temporary cure. The patient may be kept flat on his back with the head between sand-bags for several weeks, but old or debilitated patients do not tolerate this immobilisation at all well. The use of a light celluloid splint may be sufficient to restrain the spasm and to give relief in some cases. The administration of bromides is useful in many cases as an adjuvant to local treatment. In view of the fact that we are dealing with an abnormal movement and not with peripherally arising spasm, it is to be expected that motor nerve or nerve root section should give unsatisfactory results. This is indeed the case, and the original spasm being stopped by paralysing the muscles concerned is apt to be replaced by the development of comparable spasm in other neck muscles. However, occasional successes are obtained by extensive denervation of muscles, a severe operation for which old and debilitated subjects are unfitted.

F. M. R. Walshe.

PSYCHOLOGICAL MEDICINE

DEFINITION.—Psychiatry is that branch of medicine whose special province is the study and treatment of all types and degrees of mental ill-health, however produced.

Put in the most general terms, mental ill-health is experienced subjectively as a substantial impairment of comfort and happiness, and is shown objectively as a substantial impairment of efficiency, or of the capacity for satisfactory social relationships.

It is, of course, true that these effects are usually produced as the result of physical disorder or disease ; and although general medicine has in the past been little concerned with such psychological and social considerations, yet these are always important aspects of every illness, and should be considered in every case. Psychiatry, however, whilst emphasising the importance of the commonly neglected psychological aspect of illness, has no desire to claim the whole of medicine as its domain ; and it is only when the psychological aspect should be regarded as being predominant that a patient becomes primarily a psychiatric problem.

In 1945 there were 146,027 patients notified as under care in the mental hospitals of England and Wales (about 3·5 per thousand of the population), and 24,281 patients were admitted to mental hospitals for the first time.

In addition there were, in 1945, 99,608 mentally defective persons under statutory care, but this falls far short of the total number of mental defectives in England and Wales, which has been estimated at 300,000 (8 per thousand of the population). The figures for Scotland are comparable.

There are no reliable figures available as to the number suffering from minor forms of mental ill-health (frequently masquerading as physical disease) of insufficient severity to necessitate institutional care but none the less potent causes of personal misery and social inefficiency. There can be no doubt, however, that this group is an enormous one. It has even been estimated as 30 per cent. of all sick persons (Report of B.M.A. Committee on Mental Health).

When to the above is added the large army of the socially undesirable and inadequate—criminals, drunkards, prostitutes, and many more with an important psychiatric aspect—it will be realised that the magnitude of the problem which confronts psychiatry reaches dimensions much larger than that provided by any one branch of general medicine, and is comparable with that confronted by general medicine as a whole.

ÆTIOLOGY OF MENTAL DISORDER

The basic ætiological principle in psychiatry is that (i) psychological factors, (ii) physical factors, and (iii) constitutional factors must be considered in every patient.

These terms, mental, physical, and constitutional, of course, really only

denote aspects of the total activity of conscious human beings. It is, however, convenient to separate them, and to regard both normal and abnormal behaviour as resulting from the interaction of the three corresponding factors. Moreover, it must be remembered that these three groups of factors—mental, physical, and constitutional—are inevitably and invariably present and operative, though they may be regarded as varying greatly in their practical importance from individual to individual and from case to case.

Now clearly it would be unreasonable to expect either the normal or abnormal behaviour of human beings that issues from the complex series of interreactions of these three factors to be wholly explicable in terms of any one member. Thus there is never a single and simple cause for normal behaviour, nor is there ever a single and simple cause for mental ill-health.

The necessity for such a triple approach can sometimes be seen in an almost diagrammatic way. Thus a man whose mother had been in a mental hospital developed influenza, as the result of which he lost his job and became profoundly depressed. Few cases show their mixed ætiology quite so clearly, but all possess it, and it is one of the tasks of psychiatry to try to assess the relative importance of the different causes in a particular case.

Certain consequences of this basic principle of triple ætiology may now be mentioned :—

1. Since physical factors are always present, and may be extremely important in producing mental symptoms, it follows that psychiatry cannot be sharply separated from general medicine. A general medical training and a sound knowledge of general medicine are, therefore, essential for psychiatric study and practice.

2. The view is sometimes held that mental illness has always a physical cause. It is, of course, true that the development of mental symptoms can quite frequently, as in senile dementia or febrile delirium, be regarded as the more or less direct consequence of physical disorder or disease. But it would be wrong to assume that this must always be so. Psychological factors can also be extremely important ; and there is no logical or scientific necessity whatever for the assumption that mental symptoms may not result as the more or less direct consequence of psychological causes, or, for that matter, of constitutional causes. In brief, any of the three groups of factors can assume predominant importance.

3. Even when, as in senile dementia or febrile delirium, the occurrence of mental illness can be more or less directly attributed to physical causes, it will be obvious that the study of such impersonal physical factors cannot possibly account for the individual or personal difference in the mental symptoms displayed. The explanation of the individual psychological symptomatology (content) must clearly be sought in the personal biography of the individual concerned. Thus to give a crude illustration, a patient cannot harbour the delusion that electricity is played on him unless he has heard of it.

This problem of the distinction between occurrence and content, or the problem of the distinction between the ætiology of the condition and the genesis of the psychological symptoms, is a very important one. The elucidation of, for example, physical factors may throw great light upon the

former but can never throw much light upon the latter ; for psychological states can never be completely described or understood with the physical concepts of general medicine. This does not, however, imply that they cannot be approached scientifically.

4. Mental illness, of whatever origin, must have a mental aspect. This perhaps explains, if it does not excuse, the tendency to the view that mental symptoms are entirely dependent upon mental causes. This, of course, is equally as erroneous as is the view that mental symptoms are entirely dependent upon physical causes. It is very important, when dealing with mental illness, to be aware of the dangers of a spurious psychogenesis. This may result in the following way. The study of the biography of a patient often discloses psychological experiences that are clearly related to the mental symptoms he shows. But not infrequently these psychological experiences are important only as regards the origin of the psychological symptoms ; and it is very easy to make the mistake of ascribing to the psychological experiences that determine the genesis of the psychological symptoms ætiological importance in the production of the whole reaction which they do not possess, and which should be sought elsewhere in the physical or constitutional fields.

A simple illustration is afforded by a case of depression (melancholia), a condition primarily of constitutional origin which is frequently characterised by self-reproach. Now there are few who have not some cause for self-reproach ; and the particular topic of self-reproach may be given and accepted as the cause of the depression when it should really be regarded as a consequence.

Each of these three groups of factors—psychological, physical, constitutional—will now be considered in greater detail. It will soon be apparent how artificial is the separation and how much they are interrelated and overlap.

Psychological Factors.—Generally speaking, it can be said that from the psychological point of view mental symptoms are always produced by emotional disturbance, or by mental activity associated with emotional disturbance. It may often seem that something else is responsible, such as overwork ; but it can generally be shown fairly readily that it is not the overwork itself but the emotional strain under which it has been done, or which has driven the patient to undertake it, that explains the breakdown.

Normal and Morbid Emotional Reactions.—We tend to regard as normal any emotional reaction that we can readily understand as being justified by the circumstances. We can, for example, all understand the depression that follows a recent bereavement. There is, of course, no sharp line at which abnormality begins. But, put in most general terms, emotion may become morbid either (i) by reason of its intensity and duration, or (ii) because it is produced by what seems an inadequate cause.

Thus whilst a degree of depression can be regarded as the normal reaction to a bereavement, the development of a profound condition of melancholia cannot be so regarded ; similarly, whilst a considerable degree of fear is normal during a bombardment, the development of the same degree of fear becomes pathological when aroused by the task of crossing an empty street.

The Origin of Morbid Emotion.—The origin of emotional disturbance must not solely be sought in the nature of the environmental situation ;

for the reaction to the stress imposed by a particular situation will vary according to the nature of the individual exposed to it. Therefore two factors—the environment and the individual—must always be considered. Past experience helps to form but does not entirely determine an individual's nature; and, similarly, present experience helps to form but does not entirely determine his emotional response.

Psychological causes of emotional disturbance must, therefore, often be sought in the history of the individual as well as in the stress imposed by the more immediate situation with which that individual is faced; and not infrequently the experiences of more remote origin are the more important.

Inner Stress or "Mental Conflict."—Just as it would be impossible to give all the possible situations of strain that might be imposed by the more immediate environment, so it is impossible to give all the possible causes of more remote origin consequent upon past experience that may also give rise to emotional disturbances owing to inner stress or "mental conflict."

Thus there is often a discrepancy between duty and desire and between desire and achievement; and even when what was desired is attained it does not always satisfy.

This raises an important aspect of mental conflict. A patient may be and often is adequately and painfully aware of the nature of his problems; and he may or may not be able to cope with them. But often he is not accurately aware of the nature of the conflict going on in his mind; and then its solution becomes a difficult matter, for it is less easy to cope with a situation the true nature of which is not understood or which is mistakenly supposed to be other than it is.

A lack of knowledge of the factors that induce our feelings and dictate our actions is inevitably present in some degree in everyone; but this ignorance is often present in cases of mental disorder and may be an important factor in their causation.

This lack of knowledge arises because (i) introspection is not available for those factors—physical and constitutional—which are not psychological. Knowledge of these factors must at best be incomplete, inferential, and not direct; (ii) because introspection is imperfect even for those factors that are susceptible of introspection, namely, psychological factors.

It would be a mistake to suppose that introspection is normally or ever exhaustive and infallible. It is as easy, and probably much more common, to make mistakes in describing what is in or on our minds as it is to make mistakes in describing a scene in the outer world. In the one case, as in the other, desires, prejudices, and expectations will distort observation and falsify recollection, so that the real constituents of the scene will be ignored, misdescribed, or a wrong attribution of their origin will be made. These errors will occur more readily if the results of more accurate introspection or observation are disconcerting or disgusting, or damaging to the self-esteem, and thus calculated to arouse emotions of an unpleasant character.

Such a sequence of events is sometimes described as an example of *repression* into the *unconscious*.

Now if ever a word deserved to be paid overtime it is the term unconscious. Indeed, the term unconscious has been used in so many different senses that it would seem preferable to limit its meaning to that defined on page 729,

and to call subconscious those phenomena which are not remembered owing to emotional factors, or which, if recalled or available to consciousness, are not correctly recognised and correlated because their recognition and correlation would be distasteful or intolerable to the personality.

Again, repression does not mean discipline or self-discipline, but the means whereby self-protection is sought, and the preservation of self-esteem attempted, through self-deception or the adoption of the policy of the ostrich. Repression (self-deception) may, for some, be a helpful or even essential method of achieving an adjustment to life ; but for others it may be harmful and crippling, by preventing them from realising the true nature of their difficulties, which do not cease to exist because they are not recognised but which, if correctly recognised, they may be able to face and to solve.

It is startling how the inability to connect facts which are obviously related bears no relationship to intelligence. Thus a popular young curate of charm and considerable ability began to develop doubts about religion and shortly afterwards palpitations, sweating, and a feeling of collapse, at first only when called upon to preach, but later at other times as well. After exhaustive physical investigations had proved negative he was seen by a psychiatrist, when the above story rapidly emerged, and it was found that he had made no connection between his religious scruples and the development of his symptoms in the pulpit.

The significant psychological factors at work can often adequately be understood by a careful history taken along ordinary lines, and it is by no means always necessary or wise to seek for the essential psychological causes in the remote past or early childhood. Psychological delving of this type always involves two dangers, namely, either that of leading the victim along tracks which conform to the preconceptions of the investigator, or arriving at facts, attitudes, or problems which are, or which are supposed to be, so universal that they have no value in explaining individual difficulties. Such ætiological whipping-boys as the " œdipus situation " or inferiority complex can explain everything and therefore explain nothing. Indeed they approximate perilously to the explanation that would be afforded by attributing a patient's condition to his birth, which has, however, the advantage of being quite certainly true.

Furthermore, it must be remembered that, since psychological factors are never the only causal factors, psychological explanations must, of necessity, be incomplete as causal explanations. Even if they account for the particular symptoms that are shown, they may fail to explain why these occurred at the time they did. Thus the sexual offences of an early paretic may be interpreted in the light of his " mother-fixation " or his aggressive tendencies towards his father ; but such interpretative excursions do not explain why he behaved normally before the time of the offence, and worse than this, no plumbing of psychological depths can bring to daylight the (unconscious) invasion of the brain by spirochætes.

This example illustrates the dangers of purely psychological explanations, and why it is so mistaken and misleading to regard the unconscious as an explanatory widow's cruse.

The Effect of Morbid Emotion.—Emotional upset, however caused, may produce symptoms of either mental or bodily distress or both combined.

A clear recognition of the effects of the physical accompaniments of emotion is of cardinal psychiatric importance. They explain how it comes

about that so many patients who should be regarded as psychiatric problems do not complain primarily or at all of mental symptoms but do complain of physical symptoms. These patients naturally but erroneously tend to believe that physical experiences and physical symptoms have a physical origin, and do not relate their physical symptoms to emotional disturbance because they cannot see the connection, and often do not want to. Their "resistance" often arises because it is more pleasant to attribute an illness to a potent poison than to a poor personality.

Bodily symptoms of so-called functional origin will occur more readily if the physical make-up of the patient is of such a type that it readily responds to emotional disturbance. Thus certain individuals with a labile vasomotor system readily respond to emotion with tachycardia, others by fainting. They thereby provide examples of the interrelation of different factors.

Physical Factors.—By physical factors are here meant the states of physical disorder or disease that are studied in general medicine: infections, intoxications, disorders of nutrition and circulation, metabolic and endocrine disturbance.

Constitutional as well as "exogenous" physical factors can, of course, be very important in the production of these conditions; this only serves to emphasise once more how artificial is their separation. But those constitutional factors that are more directly concerned in the production of mental disorder (such as heredity) will be dealt with later.

The Physical Basis of Mental Disorder.—Sometimes mental changes can be correlated with general brain damage, as in arteriosclerotic dementia, and occasionally particular mental symptoms can be correlated with localised brain damage, as in post-apoplectic aphasia. But in the majority of mental syndromes neither macroscopic nor microscopic changes have been found in the central nervous system. It must, however, be remembered that our present methods of examination are very crude, and can as yet tell us very little of the presumptive changes in the central nervous system that accompany functional activity, normal or abnormal. Electro-encephalography (*vide* p. 648) may in time throw some light on these matters.

Indeed, unless disordered function is the result of permanent structural change in the brain, the demonstration of abnormal histological findings cannot reasonably be anticipated. It would therefore be a mistake to seek for the pathology of mental disorder only in the pathology of the brain, and it would be an even greater mistake to seek it only in neurohistopathology.

The importance of the physical changes that accompany emotion have already been mentioned; and it must be emphasised that these physical changes are just as much a part of an emotional reaction as is the mental experience of emotion of which indeed they form an integral part.

This mutual relationship and interdependency between the mental and the physical aspect is often particularly well shown in the course of a case of Graves' disease.

The Assessment of Physical Factors.—As has been mentioned, physical factors may be of predominant importance in the production of mental disorder; and there is no form of mental disorder, mild or grave, in which physical factors may not play a more or less important contributory part. It must, however, be emphasised that the importance of physical factors is

often greatly exaggerated, and that physical abnormality is often coincidental and not causal.

When physical factors are of predominant ætiological importance, as in general paralysis of the insane, the mental changes will be those of an "organic type of mental reaction," the characteristics of which will be described later.

As a working rule it can be taken that, in so far as mental changes resemble less those of an "organic type of mental reaction," and approximate to some other type of syndrome, so does the predominant ætiological importance of physical factors become suspect.

Anything, however, that lowers the general efficiency of the patient will facilitate the development of mental disorder in a susceptible subject; hence arises the importance of physical factors as a contributory cause. As the man in the street rightly believes, "worries get a hold" on those who are physically run down in a way they would not otherwise.

Physical Factors of Crude Exogenous Type.—Nevertheless, although such factors as chronic infections or intoxications, resulting from "focal sepsis" or other cause, should always be sought for and dealt with, their removal or eradication seldom produces that benefit in mental disorder that the student might be led to expect. The importance of physical factors of a crude exogenous type has been in the past, and sometimes still is, grossly exaggerated. In the majority of mental disorders no evidence can be found of "exogenous" physical factors that can reasonably be inferred to possess practical importance; and it seems probable that the physical basis for mental disorder should rather be sought in metabolic and other disturbances of a more subtle kind.

Endocrine Glands.—The vegetative nervous system and the endocrine glands exert a profound influence on metabolism, and play an essential part in the integration of mind and body. They are, therefore, of special interest in psychiatry. Although there can be no doubt about their importance, very little exact knowledge is as yet available as regards the role of endocrine glands in the production of mental symptoms. This is well shown in the sexual glands, and is all the more striking as their influence on the mind is best known.

Thus we know that the highest incidence of psychoses occurs round about puberty and the climacteric, *i.e.*, the times of the beginning and end of the reproductive period; and we know that menstruation is often accompanied by symptoms of emotional disturbance, which can in some women be serious. But we no longer firmly, if vaguely, attribute psychoses to amenorrhœa, or regard masturbation as a cause of schizophrenia. For we now regard amenorrhœa, which is very frequent in the case of major psychoses, as the consequence of the deranged metabolism accompanying them rather than as their cause; and we now realise that masturbation can be regarded as a normal phase in development, and that in schizophrenia it is often only a symptom.

Constitutional Factors.—Physique—The constitutional background may be demonstrated to some extent in the patient's physique, and attention has been drawn by Kretschmer to different types which can be observed amongst mental patients as well as in the general population.

1. *The Asthenic or "Leptosomatic" Type* is characterised by a narrow build, an angular profile, and by a lean, dyspeptic, and hungry look.

Individuals of this type look taller than they are. Their skin is poorly vascularised and pale, and the distal parts of their extremities tend to be cyanotic. They are flabby and of poor muscular development. Their chest is long, narrow, and flat. The subcostal angle is less than 90 degrees.

2. *The Pyknic or "Pyknosomatic" Type* is well demonstrated by "John Bull," with his large body cavities and generous distribution of fat about the trunk. John Bull in his younger days, if a typical pyknic, had a handsome body with a graceful motor apparatus and small and delicate extremities.

3. *The Athletic or "Athletosomatic" Type* is recognised by the strongly made skeleton and muscles and is well seen in a certain type of raw-boned Scot. It is less clearly defined than the other two, but is perhaps more definite than other types that have been described, such as the dysplastic.

There is a certain affinity between the pyknic build, cyclothymic make-up, and the development of manic-depressive psychoses on the one hand, and on the other hand between an asthenic build, a schizoid make-up, and the development of schizophrenic reactions. These facts are of interest, and may have some practical value in the assessment of certain mixed and complex mental reactions. But it must be emphasised that these associations are by no means invariable and that there are many exceptions.

Heredity.—The importance of the hereditary factor in mental disorder —and it is great—usually lies in providing a *predisposition*, which may or may not be made manifest by precipitating factors, both physical and mental. It is seldom of a simple and clearly demonstrable type, as in Huntington's Chorea (*vide* p. 613).

It is widely supposed that differences in personality or constitution are predominantly determined by a very large number of genes of small effect. "The neurotically predisposed man is then to be regarded as a man who has more than average susceptibility to environmental stresses of one or a number of kinds: he represents one of the extremes of human variation" (Slater).

A distinction must, however, be drawn between the relative roles in the production of human variation exerted by many genes of small but additive effect and specific genes of large effect. The former can provisionally be regarded as ultimately responsible for variations in intelligence and for character differences in general (amongst which a neurotic predisposition must be included), where the normal and abnormal fade imperceptibly into one another.

On the other hand, where specific genes of large effect are concerned, a reasonably hard and fast distinction between the normal and abnormal is much more likely to be observed, as in the more clearly cut syndromes of manic-depressive psychoses and schizophrenia.

There is, of course, no reason why specific genes of large effect resulting, for example, in a classical manic-depressive psychosis should not be combined with many genes of small but additive effect that may result in either a stable or a neurotically predisposed individual; and manic-depressive illnesses can afflict both types.

The more precise genetic facts concerning the more clearly cut syndromes will be found in the appropriate sections.

SYMPTOMS ENCOUNTERED IN MENTAL DISEASE

It is essential for the student to know what are the more important symptoms that may be shown in mental disorder, and that he should also be clear as to the meaning of the technical terms that have been used to describe them.

Unconsciousness.—An unconscious patient is neither aware of his environment nor capable of responding to psychological stimuli in a psychologically understandable way (*inaccessibility*). He is subsequently incapable of recalling any mental activity during the period in question. States of unconsciousness are best observed after severe concussion, in deep anæsthesia, and as a final stage of many intoxications. Between unconsciousness and consciousness there are various types and degrees of disturbed consciousness.

Disturbances of Consciousness.—These disturbances are mainly due to physical causes, and the general characteristics may be given as follows :—

1. Deficient grasp.
2. Disturbances of attention and concentration.
3. Slowness of thinking.
4. Disturbances of memory (retention).
5. Lack of goal-directed initiative in thought and action.

Consequently the patient shows :—

Disorientation.
Disconnected and often incomprehensible behaviour.
Subsequent amnesia.

Three intermediate states between consciousness and unconsciousness are often recognised :—

1. *Dimming or Clouding of Consciousness* (often rather unfortunately called " confusion ").—Less than normal rather than anything abnormal is experienced. All mental processes are slow. Association of ideas is scanty. Thinking is difficult or impossible. These patients are apathetic and bemused, show no initiative, are easily fatigued, and it is hard to attract or to hold their attention. They tend to pass into a dreamless sleep, stupor, or coma. In *mild* cases the patients may answer and behave rationally under examination, but readily relapse when left to themselves. In cases of moderate severity, although out of touch with their surroundings, they may be roused to answer simple questions correctly. And in severe cases it may just be possible to get an occasional appropriate response by forcible questioning or commands.
2. *Delirious States.*—The consciousness is clouded, and the continuity of mental processes is interrupted or shattered by abnormal experiences such as hallucinations. Restlessness is a most common feature.
3. *Twilight States.*—There is a peculiar alteration of consciousness and personality for certain periods of limited duration, with subsequent amnesia. They are mainly encountered in epilepsy (*vide* p. 767) and also, rarely, in hysteria.

Attention is the term used for describing the experience that certain objects are in the centre of consciousness, whilst others lie more towards the periphery. This distribution may be achieved either voluntarily or involuntarily. Attention may be disturbed in various ways :—

1. It may be difficult or impossible to *arouse* the attention of the patient. This generally occurs in organic reactions resulting in disturbed consciousness ; but it may also occur in states of " retardation," perplexity, or self-absorption due to depression or schizophrenia.
2. It may be difficult or impossible to *keep* the attention of the patient, (i) because the patient returns to predominant preoccupations (depression and schizophrenia) ; (ii) because the attention of the patient is readily distracted by stimuli from the outside, this distractibility preventing concentration on any given subject for any length of time (manic and certain organic pictures) ; (iii) because the attention may have been caught and kept by some incidental stimulus in the external environment from which it cannot be detached (certain organic states).

Volition, General Activity, Motor Behaviour.—*Lack of Initiative* is most frequently seen in neurasthenic states and in depressive and schizophrenic psychoses, but may also be observed in lesions of the frontal lobe or the basal ganglia.

Retardation denotes slowness of speech and action, generally combined with a poverty of impulses and tardiness of response. It occurs in depressions, and when very severe it may result in depressive stupor.

Psychomotor Hyperactivity, together with an increased speed of action, is seen in manic states. Impulses may follow one another so rapidly that none are properly carried out or completed.

In *Catatonic Excitement* the motor behaviour is generally more disintegrated, and features like *stereotypy* (monotonous repetition in speech and movements), mannerisms, and grimacing are often observed and are highly characteristic.

Perseveration, as opposed to stereotypy, denotes the repetition of a movement or action in spite of the patient's effort or desire to produce a new one. It may be most marked in the field of speech and difficult to distinguish from aphasic disturbances (*vide* p. 606). It is common in all organic states.

Stupor means complete suppression of speech, movement, and action not accounted for by profound disturbances of consciousness. It is commonly produced by schizophrenic disturbances of will, but it may result from extreme retardation in melancholic patients. *Flexibilitas cerea* (a peculiar type of " wax-like " rigidity of the muscles), *catalepsy* (the tendency to keep up postures which have been imposed), and *negativism* (automatic resistance to all outside stimuli) are symptoms that are often found.

Suggestion means influence by processes other than reason ; *suggestibility* is the capacity—varying in each individual—of yielding to such influences. This normal attribute is increased in states of disturbed consciousness. It is strikingly present in hypnosis, and in schizophrenics it may reach the extreme degree of *automatic obedience*. *Echopraxia* and *echolalia*, *i.e.*, the automatic repetition of actions which are seen, or of words which are heard, are particular examples of this.

Abnormal impulses, such as *kleptomania* (the impulse to steal), *pyromania* (the impulse to set fire to things), are better classified with compulsive or obsessional phenomena, *i.e.*, actions carried out under the subjective feeling of being forced to do them, either without or against intention or desire.

Feelings of Passivity (or of being influenced) describe those conditions when patients believe their experiences are produced by some outside agency or force, or that they are under the attempted or successful direction or control of this outside agency or force. These may range from bodily experiences, attributed to electricity, to strangely developed mental experiences, attributed to hypnotism, electrical waves, or the operation of wireless or telepathy.

These phenomena are very common in schizophrenia.

Disturbances of Thought.—*Retardation*, encountered mainly in depressive states, is characterised by slowness or difficulty in the process of thinking often accompanied by a poverty of ideas of which the patients are clearly aware. Many depressive patients who are retarded do not, however, so much complain of slow thoughts or empty minds as of thoughts that go round and round but do not get on. An extreme poverty of association may lead to a form of perseveration very like that seen in organic conditions.

Circumstantiality means slow progression of thought when due to a tendency to digress into trivial bypaths or irrelevancies. This type of thinking can often be found in epileptics, in morons, and in patients with organic diseases of the brain.

Flight of Ideas denotes a severe degree of the manic disturbance of thinking. Manic patients think quickly and have a great wealth of association; but these are superficial and often dictated by rhymes. Manic patients cannot pursue a consecutive line of thought of a purposive kind. Flight of ideas is an exaggeration of the method of thinking which Schopenhauer attributed to certain authors. "They write as if they were playing dominoes. The incidental number of the last piece determines the next, and the following piece has no relation to the last but one." An example of "flight of ideas" is provided by a manic patient who said "maternal, paternal, infernal, Dante."

Incoherence denotes the breaking up of the ordinary sequence of structure of thought into larger or smaller fragments. It is sometimes possible to discover why ideas with apparently no connection are associated with one another. The reason for such associations differ from those that govern ordinary logical thinking. Incoherence occurs in schizophrenia, when it has a particular quality, and in confusional states, as after an anæsthetic. Normal people may experience something very similar in dreams.

Blocking, or a sudden interruption in the stream of thought, occurs in schizophrenia.

Neologisms are frequently invented by schizophrenics. A patient, for instance, described a drawing: "Cordron. A theme of curved and fancy lines. stcollic st. from steeple word from the point on the top of the post collic (unexplainable) word matching the point; caller from the cordron and cross piece. Squirrel, wirrel, from wearl; the curls in the lines which look like a wearl pool."

Predominant Ideas are convictions not based on reason but on an emotional foundation. They are not necessarily pathological, and every normal person tends to develop them in the fields of politics, religion, and love.

The term "*Paranoid*" implies a resentful sense of a hostile environment coupled with a tendency towards the formation of delusions of a systematised character to explain it.

A *Delusion* is a false belief which cannot be corrected by an appeal to reason or logic. The education and environment must be taken into account in assessing whether a patient's ideas should be regarded as delusional or not. Primary (or autochthonous) delusions spring up suddenly with conviction but without previous warning, often in the setting of a peculiar tense emotional atmosphere. They are characteristic of early schizophrenia. Thus a schizophrenic became suddenly certain that the firing of cannon in Hyde Park to celebrate the King's birthday really foretold the end of the world.

Many delusions are secondary to hallucinations, but they can occasionally develop from a real event or experience as the result of systematic although emotionally biassed reasoning.

Delusions are usually classified as delusions of grandeur, of self-reproach, of poverty, of reference, of persecution, or as hypochondriacal delusions, according to their content.

Some schools of psychology try to explain their origin by invoking various psychological mechanisms. Delusions of grandeur, for example, are said to result from over-compensation to feelings of inadequacy, insecurity, or inferiority. Self-reproach is explained as incomplete or unsuccessful repression which leaves the feeling of guilt behind. Persecutory or paranoid ideas are said by some psychiatrists to represent the projection of repressed homosexual tendencies. Most authors, however, would regard this last explanation as too restricted, and would hold that any undesirable tendency or quality which could not consciously be endured by the individual may be projected and result in a delusion of persecution.

The recognition of these mechanisms, when they can be proved to exist in an individual case, may be of value as indicating how that case should be approached; but their wholesale assumption is unwise, and may prevent the investigator from seeing the really significant psychological connections in an individual case.

Indeed, they are often a mere description in other terms, and it can frequently be demonstrated that a variety of different delusions may be equally well understood by invoking the same mechanism, which limits its value as an explanation of any particular delusion. For instance, although hypochondriasis may be explained as representing the flight from environmental or personal difficulties into illness, yet this explanation is too general, and does not account for the transition from a mere preoccupation with the bodily functions to definite delusional formation, such as that the bowels are blocked or that the organs are rotting away, or that the brain is liquefying, or that the body is dead (nihilistic ideas).

Obsessional Ideas (compulsive thoughts) must be distinguished from delusions and from predominant ideas. Compulsive thoughts are recognised as being abnormal and foreign to the personality, and are resented and resisted. The patient struggles against an obsessional idea, but fights for his delusions, and accepts or revels in his predominant preoccupation. In content, obsessional thoughts are often banal and pointless, but sometimes indecent, blasphemous, or aggressive formulations may be expressed.

Disturbances of Affect (or Emotion).—The disturbances may consist of variations in intensity or duration, or the emotional response may be abnormal

because it is inappropriate in the particular situation. Some of the emotions met with in psychotic patients are of a kind either unknown in normal individuals or only experienced by them in very special circumstances.

Intensity.—Some patients show an increase in the intensity of their emotions at the beginning of an acute psychosis, others, however, complain of their poverty and loss of emotion (*affective loss*). This is common in depressions and in early schizophrenia. Again, certain quite normal individuals are acutely aware of complete emotional detachment after a psychic shock, such as seeing an accident. This is usually a transient experience of no significance. *Shallowness of affect* is frequently seen in imbeciles, schizophrenics, and in dements. In so-called moral insanity (moral imbecility) the social sense is poorly developed or apparently missing.

Incapacity to control the emotions and their expression is characteristic of organic syndromes (*emotional incontinence and lability*). Normal emotional experiences, such as elation, depression, irritability, anxiety, may become morbid by reason of their intensity and duration, but the extreme degrees of melancholy and panic are never experienced by the normal individual. *Ecstasy* may be described as a feeling of overwhelming bliss combined with an all-pervading sense of clearness of perception. It is often associated with a feeling of suspicion and fear, and not infrequently accompanied or followed by the appearance of autochthonous delusions. True ecstasy is probably beyond the experience of the imagination of normal persons. States of ecstasy are chiefly seen in schizophrenia.

Incongruity of Affect.—This is also a frequent symptom of schizophrenia. By incongruity of affect is meant, for example, that the patient may refer with indifference to the most horrible experiences, or even jest about them.

Ambivalence denotes the simultaneous existence of contradictory emotions, also frequently observed in schizophrenics.

Disturbances of Memory.—The function of remembering is generally divided into (1) Registration, (2) Retention, (3) Recall.

1. *Registration.*—Registration of the material to be remembered may be disturbed by lack of concentration. Thus in manic states the distractibility of attention prevents the patient from perceiving properly what is happening. The manic patient will therefore tend only to remember subsequently those things that by chance, or because of their special impressiveness, did not escape his attention. In states of unconsciousness nothing can be recorded, hence the subsequent amnesia. When consciousness is dimmed or clouded, only a partial or patchy recollection of what has taken place remains. This may even extend to a complete amnesia if registration was grossly deficient.

2. *Retention.*—Disturbances of retention should only be assumed if it is certain that registration and recall are unaffected. Retention for short or longer periods of time (the latter being essential for learning) may be disturbed to a different degree. The capacity for retaining visual and auditory material may also differ markedly. In general, the capacity to retain material is better if associations are present with which it can easily be connected. Poverty and slowness of association may simulate a memory disturbance.

3. *Recall.*—Recall may be either automatic or voluntary. In morbid mental conditions automatic recall is often preserved whilst the capacity for voluntary recall (*i.e.*, involving conscious effort) is frequently impaired. These phenomena can often be observed in normal individuals who are fatigued, or in the aged, and the disturbance is most marked in trying to

recall names. It is generally possible for a person to recognise something immediately which he could not recall on voluntary effort, or only to be able to recall facts when something associated with them is recollected. Voluntary effort quite often seems to interfere with recollection. This fact, which is known to everybody by self-observation, may be a prominent feature in the Korsakow psychosis. Thus such patients may be unable to recall things when asked to do so directly, but recall them readily if the problem is approached indirectly.

The ability to recall is facilitated by richness and rapidity of association; consequently poverty or slowness of association may make memory disturbances appear more severe than they really are. All disturbances of recall cannot, however, be explained as being due to loss of initiative or poverty of association. Nor should all memory disturbances be attributed to "repression," although this may play an important part in determining which material is forgotten, or rather which material cannot be recollected.

When memory impairment is due to organic brain disease this is usually shown in memory for recent events rather than for remote ones. The gaps of memory, or amnesia, consequent upon sudden damage to the brain (head injuries, epileptic fits, apoplexies) are often for a longer period than that of the actual unconsciousness. This is frequently seen in *retrograde amnesia* after injury to the brain, as when an individual cannot remember the accident or the events for a variable length of time preceding it. The amnesia for the period of unconsciousness, or of disturbed consciousness, is due to lack of registration. *Anterograde amnesia* (that is, loss of memory for a period after consciousness has apparently been regained) is due to a state of altered consciousness during the period which the patients do not remember afterwards.

Total loss of memory over a long period, or over the whole of life, is generally a hysterical symptom, and inconsistencies between the knowledge which the patient shows and that which he claims to have forgotten may demonstrate that the repressed material is very near the surface of consciousness: in other words, deliberate deceit, or a tendency in this direction, plays an active part.

A normal quality of remembering is that it tends to mould the past according to desire and to fill in defects in memory with facts which may have been there rather than with facts which are genuinely recollected; and the conviction that such false recollection carries is often very striking. When there is a pathological loss of memory, the gap is often filled in with the most elaborate fabrications. Broadly speaking, the less critical the patient, and the more active his initiative, the more capable he becomes of producing such fabrications, and of changing them under cross-examination. This is often strikingly demonstrated in the Korsakow psychosis.

The feeling of familiarity which is experienced on recognition may also, in certain abnormal conditions, be attached to facts or things that have not previously been known to the individual. This experience of "déjà vu" is known to many normal persons when fatigued or sleepy, and it may be a prominent feature in certain neurotic syndromes.

In the Korsakow psychosis, patients not infrequently get the order of past events wrong, so that the disturbance is not so much a disturbance of correct fact as of correct sequence.

The problem of time perception and its disturbances is still very obscure.

Some patients complain that time moves too fast or too slowly, or in extreme cases that it seems to stand still, or rushes on so fast that they cannot follow.

Disturbances of Intelligence.—The variation in the amount and type of intelligence is very great. Low intelligence is the leading symptom of mental deficiency (*vide* p. 754). An acquired disturbance of intelligence when irreversible is known as dementia. A moderate degree of deterioration may only be evident in an inability to adapt to new problems and situations, whilst the capacity to cope with ordinary activities and familiar tasks is still preserved. Severe deterioration interferes with the adjustment to the ordinary activities of everyday life. As regards intellectual performances, creative thinking suffers first, abstract reasoning next, until finally primitive tasks such as the definition of words or the finding of opposites or common qualities become impossible. The lower the original intellectual level, the more difficult it becomes to determine mild intellectual impairment. In attempting to do this it is always necessary to try to assess the patient's previous level from the past history of previous performance and occupation. Tests for original intellectual level are based on the fact that a patient's vocabulary gives a fair idea of his intellectual and educational level, and that this indicator is relatively resistant to mental deterioration.

Disturbances of Sensation.—*Hallucinations.*—These may be defined as sensory perceptions (mental impressions of sensory vividness) without objective stimulus. An example would be seeing a pink elephant when no pink elephant was present. *Illusions* are real perceptions falsified, an example being to mistake a dark stain on a pillow for a bed bug. These definitions may be accepted for practical purposes, but it should be borne in mind that normal sensory perception is far from being an objective picture of reality but is conditioned and modified by many personal factors, both sensory and extra-sensory. In other words, there is always a personal contribution to a perceptual situation, but the amount of this personal contribution varies enormously. This holds true for illusions and hallucinations as well as for normal perceptions.

Some anomalies of sensation may be mentioned that should be separated from hallucinations and illusions in the stricter sense. Thus distortions of visual impressions, owing to detachment of the retina, noises in the ear or labyrinthine sensations due to vascular disturbance, numbness or tingling in the extremities due to pressure on the peripheral nerves, all being disturbances of the apparatus of sensation, are better kept apart. The same applies to flashes of light, if produced by stimulation of the optic nerve, or the more complex subjective experiences produced by stimulation of the sensory areas of the cortex or cerebral pathways.

Visual Hallucinations are most commonly found in states of impaired consciousness (delirium and twilight states), and should always suggest the predominance of an ætiological cause of an organic type. Some normal individuals, however, experience visual hallucinations just before they go off to sleep (hypnogogic hallucinations). Epileptics in twilight states often complain of seeing red colours or fire, but their visual experiences may be more elaborate. Visual hallucinations in toxic and delirious reactions may range from kaleidoscopic patterns, which appear when the eyes are shut, to the most complex visions of scenes, persons, animals, and objects, either still or moving at various speeds. The impression may be vague, or very clear and detailed. The hallucinated objects may be projected in a real setting.

i.e., a man may be seen sitting in a real chair, but may be transparent and uninfluenced by any physical happenings around him. Schizophrenics may experience symbolic visions, often possessing a quality of intense significance; but visual hallucinations in schizophrenic conditions are more usually in the nature of vivid mental pictures rather than experiences which are thought to be part and parcel of the external world, and, except in acute phases or episodes, are rare.

Auditory Hallucinations.—These are most common in schizophrenic states but also occur in toxic confusional conditions. They are usually localised in the head, but may appear to come from outside. Less frequently they are located in some part of the body; this is very typical of schizophrenia. They usually occur in the form of voices of varying distinctness, and even when the exact words are not clearly heard the general import is often felt to be plain. Sometimes the schizophrenic patient recognises them as his own thoughts, made audible to him simultaneously, or anticipating or repeating what he is thinking. Noises, such as creaking, shooting, ringing, and so on, may also be heard. Auditory hallucinations often have an illusional foundation.

Tactile Hallucinations.—Tactile hallucinations are described by schizophrenic and delirious patients. The patient may feel he is being touched or blown upon, or they may take the form of a drizzling sensation of sand or dust. The genital organs are often the seat of tactile hallucinations, which may be elaborated into a belief that the patient has been the victim of rape. Some schizophrenic patients feel that their body, or parts of it, has changed in size or weight. Statements about a change in the internal organs, such as that the heart has become a stone, or that the bowels are blocked, may be metaphorical expressions, but are sometimes accepted later as statements of facts, and, in so far as this is the case, become delusions.

Olfactory Hallucinations.—Olfactory hallucinations, which always seem to have an unpleasant character, are frequently complained of by schizophrenics, less frequently by involutional melancholics, and occasionally by delirious patients.

Hallucinations have many points in common with sensory perceptions, but they also possess certain distinguishing qualities, quite apart from the absence of appropriate stimulus. Their perceptual character, or the conviction that they represent something of external origin, varies from case to case. Zucker has made experiments by trying to imitate a particular hallucination to see whether the patient could distinguish between their hallucination and the real perception of the attempted imitation. He found that, with the exception of certain toxic and delirious conditions, they could distinguish between the two quite readily. Hallucinations appear to be more obtrusive in character than perceptions, and tend to occupy the foreground of the patient's mind and to absorb his attention: otherwise the fact that patients are unable to disregard voices and other sensations that are practically meaningless could not be explained.

The content of the hallucinations is determined to a varying extent by the past history of the patient concerned. Elementary hallucinations are more easily explained on a neurological level, but more complex hallucinations of visions and voices can often be traced, as regards content, to the previous experiences, attitude, views, and fantasies of the particular patient. It is sometimes possible to distinguish the physiological from

the psychological element in their production. Thus delirium tremens patients usually see small and moving dots, as do patients with small scotomas. Their elaboration into rats, mice, or something else depends upon extra-sensory factors. Similarly, more complex hallucinations of cocaine addicts (cocaine bugs under the skin) are built around the nucleus of their tactile sensations. In other instances it is not easy to discover a sensory element in the development of hallucinatory experiences, or any illusional basis, and it may be preferable to interpret these experiences in the same way as dreams ; but no analysis of a graphical type can explain the fact that hallucinations occur at all. In order to explain this it is necessary to introduce factors that are not of a psychological type.

Depersonalisation.—Depersonalisation is " a state in which the individual feels himself changed throughout in comparison with his former state. This change extends to both the patient and the outer world and leads to the individual not acknowledging himself as a personality. His actions seem to him automatic ; he observes his own actions like a spectator. The outer world seems strange to him, and has lost its character and reality " (Paul Schilder).

The sense of the outer world being changed is sometimes known as *derealisation*, as opposed to the feeling that the patient is himself changed, which constitutes depersonalisation in the more strict sense. Depersonalised patients complain of loss of feeling, whereas observation of their behaviour shows natural emotional responses. There are, however, cases when the subjective poverty of emotions is followed by objective " affective loss."

PSYCHIATRIC SYNDROMES (REACTION TYPES)

It is essential to remember that psychiatry deals with individuals, and hence with *individual* reactions as varied as the nature and experiences of different individuals can make them. Consequently, as Adolf Meyer has pointed out, the problem of mental disorder is not exhausted by the attempted erection of categories of " disease entities " into which patients can be pigeon-holed from a diagnostic point of view.

The question to be asked about a psychiatric patient is not, therefore, " What kind of mental disease has this patient got ? " but rather, " What type of reaction does this *individual* show, and how can we understand it ? " And we can only understand it by studying the individual, his history, and his environment from many angles.

In modern psychiatry, therefore, the older conception, taken over from general medicine, of rather rigid and clearly defined " disease entities " has been replaced by the broader and more elastic conception of " reaction types " or " psychiatric syndromes " ; for although an infinite number of individual varieties must be recognised, certain broad patterns of morbid response can be discerned.

A *syndrome* is a complex of symptoms that tend frequently to be found in association.

Thus catatonic symptoms are not evidence of a disease " catatonia," but are symptoms that may, for example, be seen in organic types of reaction, and also, much more frequently, in schizophrenic types of reaction.

There is often considerable overlapping of the various syndromes, so

that one or more symptoms may be common to several types of mental disease.

Psychiatric Classification.—It was not infrequent in the past to consider the neuroses as quite distinct from the psychoses. This sharp distinction is erroneous in theory and misleading in practice. In the classification that follows the neuroses are included as subdivisions of one of the main groups :—

1. **The Organic Reaction Type.**—The main features are disturbances of consciousness and dementia. Organic factors are of predominant importance in the production of this type of reaction, which may be subdivided into clouded consciousness, delirium, Korsakow syndrome, hallucinosis and twilight states, and dementia.

The various organic causes which may result in the development of these subdivisions of the main organic reaction type will be discussed later.

2. **The Schizophrenic Reaction Type.**—The main features are progressive introversion, splitting of personality, and paranoid symptoms. The meaning of these terms will be discussed later. This reaction type occurs mainly as the result of the operation of constitutional factors, and may be subdivided into simple hebephrenic, catatonic, and paranoid varieties.

3. **The Affective Reaction Type.**—The main features are swings of mood, or abnormal mental and physical reactions to emotions, or both combined.

Constitutional or psychological factors, or both, are usually predominant in the production of this reaction type, which may be divided into manic and depressive states and anxiety states.

4. **The Hysterical Reaction Type** characterised by mental and physical symptoms, not of organic origin, produced and maintained by motives, never fully conscious, directed at some real or fancied gain to be derived from the illness.

5. **The Obsessive Compulsive Reaction Type** characterised by thoughts and actions which force themselves upon a patient's mind against his desire and into the abnormality of which he has insight.

When attempting to make a more complete psychiatric diagnosis the ætiological, *i.e.*, the assessment of the relative importance of the physical, psychological, and constitutional factors, should be distinguished from the descriptive aspect, *i.e.*, the syndrome or reaction type that is observed. Further, no reaction can be fully understood without taking the previous personality of the patient into account ; and finally the practical value of any diagnosis largely resides in the prognostic implications. For example, a diagnostic formulation that would satisfy the above criteria might be " Progressive presenile organic reaction coloured by alcoholism in a retired general with a highly aggressive pre-morbid personality," or " A transient affective reaction with hysterical features due to separation from home in a dependent, sensitive youth of a rather schizoid type and with a schizophrenic heredity."

SCHEME OF EXAMINATION

It is just as important in psychiatry as in general medicine to have a scheme of examination ; for unless a systematic scheme of examination is followed, important aspects and problems may be missed.

It must, however, be remembered that in psychiatry a good deal of elasticity is necessary in following such a scheme ; for it is not only essential

to try to establish a satisfactory contact (rapport) in the course of the examination, but the examiner must also attempt to gain an impression of the total personality of the patient.

The following items are suggested: Name, age, sex; single, married, divorced; occupation; addresses of patient and often also of correspondents, employers, doctors, relations; telephone numbers. Details of *complaint* and careful chronological *history of present illness*, obtained from patient and friends. Importance of independent accounts. See relatives first and separately.

Personal History.—History of early development; birth injuries; whether brought up by parents or not; the home atmosphere; relationship to father, mother, and other members of the family; dates of walking and talking; neurotic traits such as fear of the dark, stuttering, thumb-sucking, nail-biting, enuresis, sleep-walking, nightmares. Sleeping arrangements. School record: scholastic attainments, keenness in games, sociability, homesickness. Work record: jobs held, why taken on, how long held. reasons for leaving, financial returns. Past health: previous physical diseases or attacks of mental ill-health or "nerve" trouble. Liability to faint, blush, sweat, tremble. Effects of medical contacts, use and abuse of drugs, attitude towards health matters and bodily disturbance. Social and sex: attitude towards relations and friends. Sex information and development: sexual experiences, menstruation, menopause, marriage, pregnancies, contraceptive measures.

Interests, hobbies, ambitions. Legal difficulties including early tendency to lying or stealing. Religious and political tendencies. Fads and physical culture notions. Successes and disappointments, difficulties and quarrels. How spare time is employed; what makes life worth living.

Personality Traits.—Actions and attitudes indicating that patient was *sensitive*, *shy*, reserved, solitary, shut-in, day-dreamer, *sociable*, active, friendly, affectionate, adaptable or not, stubborn, obstinate, *suspicious*, jealous, frank, *moody*, restless, dissatisfied, irritable, impulsive, cheerful, anxious, apprehensive, *conscientious*, neat, orderly, meticulous, efficient, cruel, stingy, *hypochondriacal*, eager to have sympathy, "martyred," *aggressive*, submissive, a leader, a follower, self-confident, apt to feel inferior, *religious*, ethical, moral, interested in the abstract and in "right and wrong."

Family History.—Nervous and mental illness, epilepsy, alcoholism, drug addiction, personality traits of relatives. Moodiness, seclusiveness, successes, failures. Suicides. *Hospitalisation.* Social and cultural standing.

Mental Status.—(a) *Appearance and Behaviour*: Rapport, facial and bodily expression, condition of hair and clothing; manners, gestures, mannerisms, grimacing. Tremor, restlessness, agitation. Co-operation, distractibility; spontaneity in speech and action.

(b) *Talk*: The form of the patient's utterances rather than their content is here considered. Does he say much or little, talk spontaneously or only in answer, slow or fast, hesitantly or promptly, to the point or beside it, coherently, discursively, loosely, with interruptions, sudden silences, changes of topic, comments on happenings and things at hand, appropriately, using strange words or syntax, puns? How does the form of his talk vary with its subject?

(c) *Mood*: The patient's appearance may be described, so far as it is

indicative of his mood. His answers to "How do you feel in yourself?" "What is your mood?" "How about your spirits?" or some similar inquiry should be recorded. Many varieties of mood may be present—not merely happiness or sadness, but such states as irritability, suspicion, fear, unreality, worry, restlessness, bewilderment, indifference, and many more which it is convenient to include under this heading.

Observe the constancy of the mood, the influences which change it; the appropriateness of the patient's apparent emotional state to what he says.

(d) *Delusions and Misinterpretations*: What is the patient's attitude to the various people and things in his environment? Does he misinterpret what happens, give it special or false meaning, or is he doubtful about it? Does he think anyone pays special attention to him, treats him in a special way, persecutes him or influences him bodily or mentally, in ordinary or scientific or supernatural ways? laughs at him? shuns him? admires him? tries to kill, harm, annoy him? Does he depreciate himself in any way, his morals, possessions, health? Has he grandiose beliefs?

(e) *Hallucinations and other Disorders of Perception*: The source, vividness, reality, manner of reception, content, and all other circumstances of the experiences are important; its content, especially if auditory or visual, must be reported in detail. When do these experiences occur—at night, when falling asleep, when alone? What is the patient's own explanation? Any peculiar bodily sensations; feelings of deadness?

(f) *Compulsive Phenomena*: Obsessional thoughts, inclinations, or acts. Are they felt to be from without or part of the patient's own mind? Relation to his emotional state: does he repeat actions unnecessarily, such as washing, to reassure himself? Phobias and anxiety.

(g) *Orientation*: Record the patient's answers to questions about his own name and identity, the place where he is, the time of day and the date.

(h) *Memory*: This may be tested by comparing the patient's account of his life with that given by others, or examining his account for intrinsic evidence of gaps or inconsistencies. There should be special inquiry for recent events such as those of his admission to hospital and happenings in the ward since, or his journey to hospital or consulting room. Selective impairment of memory for special incidents, periods, recent or remote happenings.

Record the patient's successes or failure in grasping, retaining, and being able to recall spontaneously or on demand, three or five minutes later, a number, a name and address, or other data. Give the patient a short story to read and ask him to repeat it in his own words. Give him digits forward and then backward, and record how many he can repeat immediately after being told them. A normal person should be able to repeat at least seven forward and five backward.

(i) *Concentration*: Subtraction of serial sevens from a hundred (give answers and time taken). Telling the months of the year forward and backward.

(j) *Grasp of General Information*: Tests for general information and grasp, as well as for ability to calculate, should be varied according to the patient's educational level, and his experiences and interests. Suitable questions are:—

Name of the King, and his immediate predecessors.
The Prime Minister.
The Chancellor of the Exchequer.
Capitals of France, Germany, Italy, Spain, Scotland.
Six large cities in Britain.
Date of beginning and end of the last war.

These tests are not intended so much to estimate general intelligence as to see whether there has been any falling away from the patient's former presumptive level of knowledge and capacity, which has to be estimated from his life history and independent information.

(k) "*Intelligence Tests*": Standardised tests of intelligence are discussed in the section on Mental Deficiency (*vide* p. 755). The signs of intellectual deterioration will be found on page 735. The best estimate of the patient's intelligence may be gained by going over his school and work record and by discussing with him his job and his hobbies. Simple clinical tests are provided by the *definition of abstract words*, e.g., "envy" and "surprise"; by the *explanation of proverbs*, e.g., "the early bird catches the worm"; and by the *explanation of differences*, e.g., dwarf and child, or idleness and laziness.

A simple story may be told to see whether the patient grasps the point.

Specimen Story.—The Donkey Loaded with Salt: A donkey, loaded with salt, had to wade a stream. He fell down, and for a few minutes lay comfortably in the cool water. When he got up he felt relieved of a great part of his burden, because the salt had melted in the water. Longears noted this advantage, and at once applied it the following day, when, loaded with sponges, he again went through the same stream.

This time he fell purposely, but was grossly deceived. The sponges had soaked up the water, and were considerably heavier than before. The burden was so great that he succumbed.

The same remedy does not apply to all cases.

(l) "*Insight*": This is best obtained by the questions as to whether the patient regards himself as being ill; what he regards as being the nature of his illness (whether physical or "nervous" or both) and whether he thinks he will get well.

Assessment of Stability.—The best indication of stability is a patient's reaction to the test of life and objective facts, above all concerning the work record. These are more valuable than subjective impressions. Suspicion should always be aroused if a man has been much unemployed (except in certain depressed areas) or when he has failed to earn more as he grows older or has frequently changed his job. It must, however, be remembered that many perfectly normal young people change their jobs a good deal when in their teens before they settle down, and this may give a misleadingly poor impression. Again, the opportunities for work have been much better since the war, and consequently the history of the work record for the last five years before the war is more illuminating than what comes after. The reasons for changing jobs are often indicative of instability, neurotic tendencies, and lack of persistence. Suspicion should be aroused concerning those who frequently change their jobs for no good reason, or state that they did so because it was bad for their health, even if this statement is backed up by alleged medical advice. Unstable individuals often

seek " lighter work " either on their own initiative or as the result of pressure from friends or relations ; and the medical attendant is often called in to endorse these views. Again, certain unstable individuals seek outdoor work not so much because they like outdoor life as because they believe or say they were told that the fresh air would be good for them. Other suspicious reasons are finding noise trying or becoming easily fatigued. Finally, there is a group who cannot stick at a job because of difficulties that repeatedly arise with their fellow-workers or with those over them.

Apart from the work record the most valuable indication of stability is evidence of *sustained* capacity for interest and activity as seen in the spare-time occupations and hobbies. The output of physical energy of unstable individuals tends to be low, and the majority of neurotic subjects do not relish team games or activities in which they can hurt themselves. In addition, many show a morbid interest in their physical health, which may not result in actually being off work but which is felt to be a handicap to them and leads to a restriction in their activities. Many neurotics also lead a very sheltered existence because they regard themselves as sensitive or highly strung, which is for them a source of self-congratulation rather than regret ; and owing to their egocentricity many of these persons are singularly deficient in a sense of humour and take themselves very seriously, even if they are fully capable of laughing at others.

The family example and tradition are often extremely important in setting both the ethical and social standards as well as the " health-conscience " of a patient, and knowledge on these points is therefore necessary in order to understand the patient's reaction to life.

TREATMENT

General Medical Treatment.—The treatment of the various conditions of physical disorder and disease that may be relevant to psychiatric problems must be sought elsewhere, and the more specific forms of treatment that are now employed for special forms of mental disease (*e.g.*, insulin in schizophrenia) will be dealt with later in the appropriate sections.

Only some general methods of symptomatic treatment, that are applicable in many conditions without reference to the special type of the reaction or its ætiology, will be considered below.

Drugs.—Drugs are mainly used to decrease anxiety, agitation, restlessness, and excitement, and to procure sleep.

For acute excitement and restlessness, hyoscine ($\frac{1}{100}$ to $\frac{1}{50}$ gr.) combined with morphia ($\frac{1}{6}$ to $\frac{1}{4}$ gr.) can be very valuable ; but it must be remembered that hyoscine produces dryness of the mouth and anæsthesia (with its effect upon respiration), and hence great nursing care is necessary.

Continuous Narcosis may be indicated in states of prolonged agitation and excitement. The object of this treatment is to keep the patient asleep for sixteen to twenty-two hours a day, for a period of from five to ten days. The technique employed varies in different centres, but usually somnifaine (2 to 3 c.c., b.d.) is given by intramuscular injection at 9 A.M. and again between 4 and 7 P.M. When necessary paraldehyde is given in the interval, either by the mouth or by rectum. The times, just before the injection, when the patients are relatively awake, are used for nursing care (bowels,

food and fluid, temperature, blood pressure, urine examination, etc.). It is essential that the patient should receive sufficient nourishment, and that it should possess the necessary caloric value.

Continuous narcosis is not a form of treatment that should be undertaken without previous practical experience. It has very great value in many of the acute reactions of war time.

For lesser degrees of anxiety and restlessness bromides may be of value, but the danger of bromide intoxication should always be borne in mind, as this may occur even with small doses if continued for a long time, especially in elderly or arteriosclerotic patients. Bromide and chloral hydrate is an excellent combination ; the latter is an excellent sedative and hypnotic, and is not cumulative in its effects. The barbiturates are also of value in states of tension. Barbital (veronal) given in divided doses of $2\frac{1}{2}$ gr. b.d. or t.d.s. often gives relief if the state of anxiety or tension is not too severe. Some patients also find the barbiturates useful to fortify themselves when likely to be confronted with a difficult situation.

Tincture of opium (dose 5 minims t.d.s., increasing by 1 minim daily up to 15 minims t.d.s.) may be given, under careful supervision, for endogenous depression with much anxiety.

For *sleeplessness* paraldehyde, were it not for its unpleasant taste and smell, would be the ideal hypnotic, for it is safe, powerful, and acts quickly. It can be given by mouth in 2-drachm doses or 4 drachms by rectum. Many of the barbiturates are also excellent : perhaps luminal (1 to 3 gr.) and medinal (5 to 10 gr.) are the most commonly used.

It is important to give barbiturates in sufficient doses, and to be ready to change them if individual intolerance is shown ; and it is often wise to combine them, *i.e.*, to order one that induces sleep rapidly with another that has a more prolonged effect (evipan or nembutal plus veronal or luminal).

In prescribing hypnotics it is, of course, essential to discover whether the trouble lies in going off to sleep (as in anxiety states), or in waking up early (as in a depressive state), or in both (as in mixed states), and to prescribe accordingly.

Bromide is not a hypnotic, but may help to induce sleep by decreasing worry and restlessness.

Benzedrine (5 to 20 mg.) has been used as a direct stimulant in patients with lassitude, depression, and retardation.

Narco-analysis and Abreaction.—Narco-analysis, essentially a time-saving device, may be called for when a patient shows psychogenic symptoms, the origin and nature of which are not obvious to the doctor and patient after reasonably extensive inquiry and ordinary persuasion. It is of particular value in the elucidation of certain hysterical conditions such as amnesia and the discovery or failure to discover hysterical motivations for the continuation of symptoms. Sodium amytal or pentothal is administered until the patient can be persuaded to speak more readily. Apart from its value in investigation, the administration of hypnotic drugs can be used in a more directly therapeutic way for the abreaction of pent-up emotional material, and many workers prefer the use of ether for this purpose. The main indications for these abreactive techniques are conditions where the trouble is largely due to the repression of painful traumatic memories or experiences. It must be realised that both narco-analysis and abreaction only constitute one step in

treatment and that all patients will subsequently need psychotherapy and re-education.

Modified Insulin Treatment.—Loss of weight is a frequent finding in many types of psychiatric illness and an impaired state of nutrition is a powerful contributory factor in aggravating or prolonging such illnesses. Insulin, in sub-comatose doses starting with 20 units and gradually increasing to 50 units or more, is of great value in stimulating the appetites of patients with loss of weight or who are physically run down. Patients are only allowed to develop the symptoms of mild hypoglycæmia which consist mainly of sweating, and sweetened tea and a meal high in carbohydrates are given three hours after the injection ; this is followed by ample food during the remainder of the day. The treatment is given on six days a week and continued for three or four weeks if necessary. The improvement in the general physical health can be very striking and is often accompanied by an equally striking improvement in the patient's mental state. It is necessary to have some experience of the symptoms of hypoglycæmia, since patients vary in their sensitivity to insulin, but with reasonable precautions the treatment is perfectly safe. Small doses of insulin often prescribed, *e.g.*, 5 to 10 units, serve no useful purpose whatever.

Shock Treatment.—Further mention will be found of insulin shock treatment in the section on Schizophrenia. This form of treatment must be given by an experienced worker with a trained staff. Electrical Convulsion Therapy (E.C.T.) has revolutionised treatment in many psychiatric conditions, particularly depressive states of endogenous type (*vide* p. 782), and it is particularly valuable in the older age groups. With suitable precautions, which must include a properly trained team of workers, it can be given to out-patients. In this treatment an electrical current is passed through the head and a major epileptic fit is produced. The main complications are fractures, and the frequency with which these occur is largely a reflection of the technique employed. The number of physical contraindications to E.C.T. have been further reduced as the result of the administration of curare. Since to be paralysed with curare is a very alarming experience, it is customary to make the patient unconscious by giving him pentothal before. Curare so damps down the severity of the fits that the physical strain is minimised. It is now, therefore, possible to treat patients with relatively recently united fractures or even with severe hyperpiesia and myocardial insufficiency. Increasing experience shows that the frequency with which E.C.T. should be given is largely an art. Acute psychoses may need the treatment daily during the earlier part of their illness, mild cases treated in out-patients perhaps only twice or three times a week to start with. The spacing of the treatment depends upon the response. In out-patient work perhaps six treatments in all would be about the average ; some severe cases under hospital care need up to ten or twelve or even more. A number of patients complain of memory disturbances whilst receiving E.C.T. treatment. They should be warned of this possibility, since it may worry them when it occurs, and they can be reassured that it is a transient phenomenon.

Prefrontal Leucotomy.—In this operation a burr hole is made on either side in the temporal region and a suitable instrument is introduced with the object of severing as many of the white fibres as possible going to and from the frontal poles. The instrument is pivoted first upwards and then downwards in a plane just anterior to the anterior horn of the lateral ventricle.

The operative mortality is about 3 per cent., the main danger being hæmorrhage. After the operation the patients may be restless and disturbed, but are usually apathetic and confused, frequently with incontinence, for a variable period. Put in the most general and rather crude terms, the results of the operation are (i) to reduce tension and (ii) to release inhibition, the valuable effects being dependent upon the reduction of tension and the unfortunate results being dependent upon the release of inhibition. The intelligence of the patient, as judged by intelligence tests, does not seem to be materially affected, but there is always some change of personality. In other words, patients always pay a price for the benefit they may derive. On the whole, very few patients indeed are worse, and the benefit that can be derived is often most striking.

Prefrontal leucotomy is not an operation that should, however, be advised until all other methods of treatment have been employed. There can be no doubt about its value in many chronic psychoses and, as a result of the operation, many chronic inmates of mental hospitals not only become easier nursing problems but are happier even if they may not be able to leave the hospital. The operation is also of value in a number of chronic depressive states who have failed to respond to E.C.T. or who cannot maintain the response they have made to E.C.T. The number of patients with depressions who do not respond to E.C.T. is rather larger than the student might suppose from perusal of the literature.

Leucotomy may also be well worth trying on certain chronic obsessional conditions with tension, and in a variety of other neurotic states with tension whose life is miserable and who cannot be helped in other ways. Finally, leucotomy may be of value in certain cases of intractable pain. The results obtained are also dependent upon where the cut is made, more profound personality changes apparently tending to occur when it is made far back. It is well to remember that the results must be judged not entirely in terms of the previous personality of the patient prior to his illness, but account must also be taken of his condition at the time of the operation and his probable outlook for the future without leucotomy. A great deal will depend upon post-operative rehabilitation, and the final outcome cannot be judged until many months after operative procedure. For example, patients often show far greater advance in the second six months than in the first.

General Management and Nursing Care.—Cases of major psychoses, especially when acute, should be confined to bed. Milder degrees of tension and restlessness also frequently respond well to this simple measure. Continuous baths at body temperature are indicated in severer forms of restlessness and excitement, though some now question their usefulness.

Padded rooms or cells are seldom used in modern mental hospitals, but were formerly employed in cases of severe excitement not otherwise controllable. It could be urged that they had a definite value for a certain type of case, and perhaps would still be used were it not for their unfortunate appearance and reputation.

It is often advisable to treat patients in single rooms rather than in large wards, for certain depressed patients are distressed by the noise made by other patients, and excitable patients are unduly stimulated and distracted by company. Separation, however, makes supervision and observation more difficult, and the treatment of suicidal patients in single rooms demands a large staff.

The ingenuity and inventiveness of *potential suicides* can never be overestimated. Some of the dangers can be guarded against by suitable planning and construction of the building, and by the adoption of certain measures in ward routine ; but strict and constant supervision, combined with knowledge of the individual patient, are probably the most effective measures. *Refusal of food*, or of sufficient food, is common in mental disorders, and may be a disguised form of suicidal attempt. If it is impossible to induce the patient to take sufficient nourishment by other means, recourse should be had to tube feeding without undue delay. Certain patients who do not refuse food entirely, underfeed themselves systematically. It is essential to keep an exact weight chart and, if necessary, to start tube feeding should the weight continue to drop.

Psychological Treatment and Psychotherapy

It has already been emphasised that the psychological effects of past experiences play an important part in every abnormal mental reaction. Environmental factors do not cease to operate after the onset of mental disorder, but continue to exert a profound influence.

It should be remembered that psychotherapy, as the term is generally understood, is only one example of an environmental influence that may produce a beneficial psychological effect, and that there are other extremely important methods of giving treatment that must be regarded as psychological treatment.

In these methods of psychological treatment the object is to modify environmental factors in order to provide satisfactory environmental conditions and opportunities, rather than to deal entirely with the individual ; both these methods of approach should always be combined.

It should be recognised that these other methods of psychological treatment may be safer, quicker, cheaper, technically easier, and that their results may last longer than treatment by major psychotherapy alone ; but, of course, in order to employ them correctly it is essential to have a thorough knowledge of the problems of the individual concerned.

General Psychological Management.—*The Immediate Environment.*—Even severe and chronic psychoses respond to changes in their environment, such as being transferred from one ward to another, or from one hospital to another. The insistence on personal cleanliness and manners has a profound effect even upon the behaviour of deteriorated patients. Milder cases are even more susceptible to the influence of their surroundings.

Admission to a hospital involves, apart from anything else, a sudden and complete change of environment ; and how fundamental a change in the clinical picture may result from this simple measure strikes even the experienced psychiatrist again and again. After admission the greatest care should be devoted to the question of which ward the patient should be in, or whether he would be better in a single room ; and as to whether he is influenced in a favourable or unfavourable way by another patient, or by a particular nurse. In brief, the reaction of the patient to his environment must be studied most carefully and the desirable alterations made in so far as that is possible ; and it is possible to a surprising extent.

Occupational Therapy, which is of cardinal importance in the treatment of mental disorder, is based on the elementary principle that it is a good thing

for everybody, including patients, to have something to do. The name is perhaps unfortunate as tending to emphasise the aspect of filling in time, whereas stress should be laid on the far more important aspects of relieving unhappiness or discomfort by distraction, affording an opportunity for the recovery of real pleasure in activity, increasing self-confidence by tangible evidence of a capacity that had been doubted, and often enough frank training in better habits of concentration and work.

Patients suffering from mental disorders often experience difficulty in making decisions, lack self-confidence and initiative, and show a loss of interest, except, perhaps, in their own symptoms. To ask such patients to plan their day, and to fill in their time as they think best, is not merely to ask something that is stupid and unfair, but it is to permit something that may be positively harmful.

Consequently, a carefully planned day, with facilities for the development and enjoyment of as many interests as possible, should form an essential part of the life in every modern mental hospital; and the same principle of careful individual planning of the best "twenty-four-hour day" that can be worked out should be applied to psychiatric patients who are not in mental hospitals.

"Occupational therapy" is not achieved by suggesting a little knitting as an alternative to brooding, or the depressing comparison of rival discomforts with other patients. It should be definitely organised; thus, for example, patients should be made to go to "occupational classes" for various handicrafts. But games and entertainments are just as much a part of an occupational scheme as raffia work or carpentry, and there are other forms of valuable, practical, and interesting activities besides indulgence in the arts and crafts.

Environmental Adjustment and Social Work.—In the treatment of out-patients, as well as in hospital cases, a great deal may be accomplished by "social work" of various kinds. The assistance of trained social workers is of the greatest value for this purpose; and many of the activities of a good general practitioner are essentially of this nature. All practitioners would be wise both to acquaint themselves with, and to avail themselves of, the social service facilities in their neighbourhood, such as welfare organisations, clubs, and recreational opportunities.

It is necessary to establish contact with relations, friends, and employers in order to get to know, and, if possible, to adjust conditions both at home and at work in a more satisfactory manner; not infrequently as much can be done by explanation and advice to those with whom the patient lives, or with whom he comes into contact, as by a more direct approach to the patient himself.

Occupational maladjustment becomes a serious problem when men are forced by economic conditions, or by their call up for the Services, to undertake work for which they are not fitted. Psychological selection, taking into consideration not only the individual's general intelligence and special aptitudes but also his temperament and character, can do much to reduce this source of mental ill-health, and also if it has suffered, to restore it.

Minor Psychotherapy.—In many instances quite simple explanation and discussion of the problems, and of the nature and origin of the illness, may effect great improvement. The patient may be given direct advice so far as certain personal and social difficulties are concerned; but it is preferable to do this indirectly, by helping the patient to make his own decisions. Sexual

problems, at the time of puberty or after marriage, or fears of pregnancy, and subsequent neurotic reactions, can frequently be dealt with by explanation and instruction, or by referring the patient to a birth-control clinic.

The suggestive influence of the personality of the doctor, and of the atmosphere of the hospital or consulting room, are factors that are difficult to assess in any kind of medical treatment. Deliberate use can be made of these influences in treating minor psychological troubles. So-called indirect suggestion by means of the electric current or inert medicines is not a very desirable way of carrying out psychological treatment ; but it can be very effective, and if it is done conscientiously, and followed up by or combined with explanation and reassurance or whatever may be necessary, it may be a time-saving method.

Persuasion, though sometimes thought to be a method of influencing the patient by reasoning, always contains a large element of suggestion.

The most striking method of treatment by suggestion is hypnosis, which is a sleep-like state in which the contact between physician and patient (rapport) is not interrupted. A person in a hypnotic state is particularly susceptible to suggestion ; and it is possible by hypnosis to influence many physical and mental functions that are not within the control of the will.

It is not possible to detail here the various methods of inducing a hypnotic state, but it must be remembered that only a proportion of mankind can be hypnotised. The therapeutic application of hypnosis is limited even for these. It is, however, an excellent method of removing hysterical symptoms, such as blindness, aphonia, paresis, or amnesia. The removal of a hysterical gait in a single session provides one of the most striking successes that a psychotherapist can have. Some patients, otherwise refractory to hypnosis, can be readily hypnotised after a moderate dose of a hypnotic. A further development is the production of a drowsy suggestible state by the administration of evipan or sodium amytal intravenously. This " narco-analysis " has proved particularly useful in the clearing up of psychogenic states of loss of memory, and it is also a convenient time-saving method for removing hysterical conversion symptoms.

Major Psychotherapy.—The more complex abnormal mental reactions constitute the main field of major psychotherapy.

Neurotic illnesses of long standing always tend to become increasingly complex, for with the passage of time, neurotic reactions give rise to new problems, which again become the source of new conflicts and difficulties. The task of trying to achieve continued readaptations to difficult circumstances often necessitates changes of attitude and sacrifices of desires, ambitions, and convictions. This may result in conscious inconsistency and strain, or repression and self-deception.

Conflicts involving deep-seated religious, moral, and social standards are not likely to yield to suggestive therapy or environmental adjustment in highly differentiated individuals, and may therefore demand more prolonged psychological treatment.

Strangely enough, psychotherapists have separated themselves from the rest of psychiatry, and occupy a position to which there is no equivalent in any other branch of medicine—hæmotherapists, or perhaps rather ferro-hæmotherapists, are unknown. This may have arisen partly owing to the large amount of time and concentration required for prolonged psychological treatment, but is probably due mainly to the formation of special psycho-

therapeutic schools, each of which has developed not only a technique but a doctrine of its own.

Psycho-analysis, based on Sigmund Freud's pioneer work on the study of the individual neurotic patient, has outgrown its character as a method of treatment, and has become a school of philosophy and psychology whose pupils also carry out psychotherapy, but only according to the strict rules of their order. The ideas of Freud, whether accepted or rejected, have given a great stimulus to psychiatric work. Their therapeutic application must be studied in the books of the master and his pupils, and the real technique is only available to the formally initiated. It is difficult to assess the results that have been claimed, for so few have been published, but they do not seem to be better than those achieved by less laborious and expensive methods.

The schools of Adler and Jung are offsprings of the Freudian psycho-analysis, whose legitimacy is not accepted by the parent. The student who takes a special interest in them must also be referred to the larger textbooks, but would do better to consult the works of those authors themselves.

The psychotherapy of the neuroses should always be based on some general principles, which can merely be outlined here very briefly. Psycho-therapeutic technique can be learnt as little from books as can surgical technique.

The first step in any form of psychotherapy must be to obtain a careful and detailed history. It is essential to collect information from all possible sources, such as relatives and friends, in order to supplement and to correct the account given by the patient himself. The collection of facts should precede attempts to interpret them ; and the elucidation of the more fundamental problems that lie behind the overt complaint or complaints is only possible in the light of these facts. At the same time it must be borne in mind that good history-taking inevitably involves therapeutic work. The opportunity of talking about intimate matters to an impartial witness is often felt as a great relief. The interviews with the doctor leads the patient to a more systematic survey of his difficulties. He has to formulate his problem in words, and by this very process they often become more clear, and can be viewed more objectively.

It is often possible, during even the preliminary period of history-taking, to remove at least some of the manifest symptoms by reassurance, suggestion, or other form of symptomatic treatment ; and this may enable the patient to face his other difficulties and problems with greater ease.

It is useful to have in mind a list of important topics in order to arrange in a systematic manner the material that must be collected in a more detailed analysis of the patient's personality. Diethelm suggests the following headings :—

1. Intellectual resources.
2. Emotional tendencies and temperament.
3. Volition and action tendencies, interests, and strivings.
4. Standards.
5. Attitude to the body and to the instinctive desires.
6. Attitude to material needs.
7. Attitude to oneself and ability to deal with oneself.
8. Social needs and adjustment to the group.
9. Assets and handicaps and personality synthesis.

There are various methods of ascertaining and of making the patient aware of the psychological factors which, for his own good reasons, he has removed from the centre of his consciousness. The choice as to whether hypnosis, free association, and dream analysis are used to supplement systematic questioning will depend upon the personal technique of the physician, on the nature of the particular problem, and upon the necessary economy of time.

The more active part of treatment begins with the explanation and interpretation of the symptoms. These, if possible, the patient should be guided to find and elucidate for himself. He is thus gradually led to a more just appreciation of the true nature of his problems and as to how they arose ; and it is well to try to discover potential assets that have not been properly utilised, and not only to dwell on the mistakes that have been made or the deficiencies that have been shown.

Some schools of psychotherapy teach that the mere disentanglement of the origin of difficulties has a curative effect. Lack of therapeutic success is ascribed to lack of depth of the analysis, and this leads to attempts to find the " essential " cause in the increasingly remote past.

This " buried treasure " school of psychopathology, the simple faith in the original psychic trauma which explains all and which, if unearthed, leads to cure, is, in its extreme form, a small one ; but in modified forms it is perhaps still all too common. It must always be remembered that the psychologically comprehensible is not necessarily the same as the causally significant (*vide* p. 725), and that understanding of the remote past does not necessarily confer control of the present. The majority of experts agree that another synthetic and constructive part of treatment has to follow. To gain a more just appreciation of the origin and the nature of the problems and to be able to assume a more detached attitude towards them means some progress ; but in order to solve them more is needed. The majority of patients need to develop new attitudes and new ways of attacking their difficulties before they can deal with their particular situation.

Only a minority of patients, or indeed of mankind, are able to develop a philosophy of their own ; and therefore the majority are more willing to accept a ready-made system and faith. These are offered not only by religion but by the various schools of psychotherapy and their adherents. The rapport developed in the course of prolonged psychotherapy often makes the patient accept the views and attitudes of his physician, be that intended or not. It must be the final object to loosen the patient's attachment again to such an extent that he is able to adopt his new insight and philosophy as truly his own, and to stand on his own feet.

For further information "Treatment in Psychiatry," by Oscar Diethelm, New York, 1936 (Macmillan Co.), is recommended.

CONSTITUTIONAL ANOMALIES

Personality, as that term is used here, comprises both intelligence and character. The personality of the patient is a very important factor both in producing and in colouring abnormal mental states. The extreme variations are often called " abnormal," an ambiguous term, used both to describe departures from the statistical average (as in the case of height) as well as

the pathological (which, as in the case of teeth, may be statistically "normal" enough). Abnormality of temperament and character may merely represent one of the extremes of human variation.

It is possible to outline only a few types of anomalies of instinct and of abnormal characters liable to become psychiatric problems. Our knowledge of intellectual deficiency (mental defect) is more advanced. This is no doubt partly because the practical importance of the problems raised by mental defect is more obvious and striking.

Anomalies of Instincts.—Although anomalies of the sexual instinct are probably the most frequent, it must not be forgotten that anomalies in other instincts, such as that of self-preservation, may also be found. Thus there are families in which a large proportion of the members die by their own hand. It is difficult to attribute this fact entirely to family example and family tradition, important though these may be. It seems more reasonable to assume that in such families the self-preservative instinct is constitutionally weak.

Sexual Anomalies.—The student should have some knowledge of normal sexual development and of the intensity, fluctuations, and variations of the sexual instinct in order to form an opinion about anomalies of time of onset, frequency, and type of sexual activity; and only very gross departures from what is statistically frequent should be regarded as abnormalities from the medical standpoint.

Sexual immaturity is the most common sexual anomaly, which, though seldom calling for medical treatment in itself, can frequently be shown to be the foundation of many types of sexual maladaptation which do call for medical advice.

Masturbation is a normal transitional stage of sexual development, but its persistence is often a symptom of immaturity. The incapacity to find a sexual partner may be only an expression of general developmental retardation. Similarly, frigidity in women is often a sign of, or results from, constitutional immaturity. The lack of desire for children may be due to the same cause. The underdevelopment of the secondary sex-characters often suggests the constitutional origin of these psychological manifestations.

The importance of constitutional factors in the production of homo-sexuality varies greatly. Homo-sexual tendencies may often be observed in various members of the same family. It may be found in men with a feminine physique or in women with a masculine physique. On the other hand, many individuals who previously showed no evidence of homo-sexual tendencies indulge in homo-sexual practices when placed in special circumstances, such as on board ship, or in prison. Such individuals have clearly been influenced by example and seduction. Homo-sexual practices are not therefore the criterion of a homo-sexual constitution, and the fact that the majority of homo-sexual prostitutes are hetero-sexual subjects proves this very strikingly. Again, many constitutional homo-sexuals never indulge in homo-sexual activities, in the strict sense, for fear of the legal or social consequences.

The typical homo-sexual is soft-natured, sensitive, and shy, and his "mother-fixation," which is sometimes alleged to be the cause of his homo-sexuality, may be regarded as one feature of his character. The homo-sexual may show feminine traits, both in physique, gesture, and in his interests.

The attraction to the same sex often seems to spring from the enthusiastic friendships so characteristic of the age of puberty, and when the relationship remains on this level, whether intentionally or unconsciously, most valuable and permanent friendships may result. But when abnormal sexuality is repressed, or when manifest conflicts with public opinion threaten, neurotic reactions often develop which bring the individual to the psychiatrist. It is not possible to describe abnormal sexual practices in detail, though they are of interest here because they so frequently possess a constitutional background. The majority of them (exhibitionism, sadism, masochism, and so on) can be regarded as exaggerations of normal sexual features that become evident when the development of inhibitions and adaptation does not reach its ordinary level. These anomalies come under the care of the physician when they give rise to conflicts with society, or if they become perversions, *i.e.*, when they dominate the sexual life instead of being part of it. It is a gross mistake to regard as perversions normal manifestations of sex. Thus to speak of infantile sadism and exhibitionism leads to wrong conceptions.[1]

Abnormal Characters (including Psychopathic Personalities).—The term "psychopathic personality" has been used to designate every conceivable type of abnormal character. The majority of psychiatrists seem, however, to prefer to restrict the use of this term to a group of abnormal individuals who exhibit persistent or repeated disorders of conduct of an anti-social type as an outstanding characteristic. The extreme psychopathic personality shows a persistent abnormality of character with explosive emotional outbursts and asocial or anti-social behaviour, but many abnormal characters do not display this triad, and amongst them may be mentioned the following :—

The *schizoid* character is not a uniform type. The abnormal characters found in the families of schizophrenics (which is the original meaning of the term schizoid) comprise shy, introverted, and secluded characters, nature-loving, abstract-minded, and idealistic, as well as cool, ruthless, remote, and egotistical individuals, and many of the queer, eccentric, and odd. The dreamy, bearded, be-sandalled denizen of Bloomsbury or Montmartre is often a schizoid, just as much as is the wild-eyed fanatical adherent of some political or religious sect. Paranoid features, either of the more aggressive or the more passive kind, are also common. There is some positive correlation between schizoid characters and an asthenic or athletic physique.

Cyclothymic (cycloid) personalities frequently occur in the families of manic-depressives. They are extroverted, good-natured, sociable, and adaptable. There is a strong positive correlation with the pyknic build : "the 16-in. neck in a 14-in. collar."

An excitable, aggressive character is sometimes seen in epileptic patients, and it has therefore been suggested that these personalities should be called "epileptoids." The relationship to this disease is, however, much less close than in the other two groups, and it seems preferable to speak of excitable or explosive types. These personalities are common in certain families, and may have a considerable importance in psychiatric practice, for criminality, suicide, and psychogenic reactions of various kinds often develop on this constitutional background.

The *hysterical* character should be clearly distinguished from hysterical

[1] A good introduction is "Psychology of Sex : a Manual for Students," by Havelock Ellis, London, 1934. (William Heinemann.)

(conversion) symptoms, for they may be observed independently of one another. The cardinal feature of the hysterical character is the desire to appear more than he (or more frequently she) really is, with which is coupled a striking skill in self-deception. Hysterics are generally easily influenced by persons or ideas that appeal to them, and they have a remarkable capacity for identifying themselves with others, and for imitating them. Their emotions are easily roused, and they express their willingness to dedicate themselves to various ideals, until their enthusiasm changes for something else, which they then take up with the same conviction. The instability of their emotions, their vivid fantasy, and the adaptability of their minds make them untruthful and unreliable, although subjectively they feel quite candid, deceiving themselves much better than they usually deceive others. They are immature in their thinking and in their emotional reactions, and the sexual frigidity, which is very frequent, may be another expression of the same fact. They are often incapable of permanent affection or sexual relationships ; but they are good short-time flirts, and know how to dally with the other sex to satisfy their vanity. Hysterical conversion symptoms often provide the means by which they try to dominate their surroundings, with varying degrees of success.

The *obsessional* (anancastic) character is not always traceable in the history of patients with obsessional neuroses, and obsessional traits are often found in the early history of patients suffering from other types of abnormal mental reaction. Obsessional features are usually described as including excessive cleanliness or tidiness, pedantry, conscientiousness, and inconclusive ways of thinking and acting. It is only when these are accompanied by the feeling of subjective compulsion that they become obsessional symptoms. The exaggerated concern with the regularity of the bowels or other excretory functions accounts for the name " anal-erotic " given to this type of character by the Freudian school. The obsessional character, as such, rarely gives occasion for psychiatric interference.

Before turning to the more definitely psychopathic personalities there is a group who may perhaps best be described as *vulnerable personalities*. These individuals, handicapped by their constitutional loading, have small emergency reserve, and when pinched by circumstances are liable to develop almost any type of neurotic reaction as well as those uncontrolled explosive emotional outbursts usually designated psychopathic. The assessment of the degree of vulnerability naturally presents difficulties, but it can be estimated with some degree of accuracy from a careful scrutiny of the past history (*vide* p. 741, Assessment of Stability).

The most common but most vaguely defined abnormal character is the *unstable psychopath*, perhaps better described as the " inadequate " person. The most prominent features are poverty of will power and determination, and this is generally shown best in the careers of such creatures. They are as debris upon the sea of life, floating from job to job and frequently submerged. It is striking to see how they can improve under strict guidance, not rarely under the thumb of a suitable wife. Unstable individuals of this type are candidates for all sorts of psychogenic reactions, and they often come under psychiatric observation because of suicidal attempts. They fill the ranks of minor criminals and prostitutes. They are often asthenic in physique, and get easily tired on physical effort ; their emotions do not go very deep, and change easily.

The *aggressive psychopath* is generally seen because he " loses his temper." He may commit serious crimes of violence. Not every person who loses his temper should be regarded as a psychopath, and the term should be used for a comparatively small group whose life history demonstrates that education, discipline, and punishment are ineffective in improving their powers of self-control. In some cases the aggressive anti-social behaviour shows periodic exacerbations. A considerable proportion of aggressive psychopaths show an abnormal electro-encephalogram, demonstrating the constitutional basis of their abnormality.

Anti-social psychopaths, or " sociopaths," are personalities who have not developed and seem incapable of developing these social inhibitions which life in society imposes on the citizen. Many persons in the present population belong to this group.

It is perhaps worth mentioning that bodily anomalies frequently coexist with the psychological anomalies in these abnormal characters and all the so-called nervous symptoms, such as tremor, restlessness, profuse sweating, vaso-motor lability with blushing and fainting, and an allergic disposition are frequently found combined with the psychopathic anomalies, though detailed correlations have yet to be made. The same is true as regards morphological anomalies, often called stigmata, asthenic build, disproportion in physique, under-development of the secondary sexual characters, or hetero-sexual features.

Mental Deficiency

Mental deficiency means intellectual defect existing from birth, or from the early years of life. Legally it is defined as " a condition of arrested or incomplete development of mind existing before the age of eighteen years, whether arising from inherent causes or induced by disease or injury." *Amentia* is a term used as a synonym ; *dementia*, as opposed to it, means intellectual defect acquired later in life. Though mental deficiency should be clearly distinguished, on principle, from psychopathic anomalies, there is no doubt that the vast majority of defectives also show anomalies in the sphere of emotion, volition, and instincts. On the other hand, a low intellectual level, even if not reaching legal deficiency, is always a serious complication of mental instability.

Mental defectives are usually graded, according to their intellectual level, as idiots, imbeciles, and feeble-minded persons (morons). The following legal definitions are useful and sufficient for all practical purposes :—

1. *Idiots.*—" Persons so deeply defective in mind from birth, or from an early age, as to be unable to guard themselves against common physical dangers."

2. *Imbeciles.*—" Persons in whose case there exists from birth or from an early age mental defectiveness not amounting to idiocy yet so pronounced that they are incapable of managing themselves or their affairs, or, in the case of children, of being taught to do so."

3. *Feeble-minded or Morons.*—" Persons in whose case there exists from birth or from an early age mental defectiveness not amounting to imbecility, yet so pronounced that they require care, supervision, and control for their own protection, or for the protection of others, or, in the case of children,

that they by reason of such defectiveness appear to be permanently incapable of receiving benefit from the instruction in ordinary schools."

4. *Moral Imbeciles.*—" Persons who from an early age display some permanent mental defect coupled with strongly vicious or criminal propensities on which punishment has had little or no deterrent effect."

Low-grade defectives, constituted by groups 1 and 2 above, very frequently show in addition physical abnormalities, and a large variety of neurological symptoms. Apart from masturbation, idiots rarely show any sexual activity. This is of interest with regard to the question of their sterilisation.

Intelligence tests, devised to grade normal and subnormal intelligence, are based on Binet-Simon's method or standardised against their scale. The Binet-Simon test consists of groups of questions, arranged for years of age, and standardised in such a way that a normal child is able to answer all the questions of his age group. The extent to which the patient answers the questions correctly determines his " Mental Age " (M.A.). The M.A. divided by the actual age of the child and expressed as a percentage gives the Intelligence Quotient (I.Q.). An I.Q. between 90 and 110 should be regarded as normal.

There are many modifications and revisions of the original test ; non-verbal (performance) tests have been proved to be a useful supplement.[1]

In an adult a " mental age " under three is generally accepted as the limit of idiocy. But the lower the intellectual level, the more doubtful becomes the value of these tests.

Imbecility is assumed up to a " mental age " of seven. This group also frequently shows physical and especially neurological symptoms. Speech is generally retarded and articulation is often poor. Emotional factors are most important in determining the patients' capacity for adjustment. Placid, manageable, docile types may be trained to some sort of work in spite of a low intellectual level, whereas excitable, restless types of higher intellectual resources may remain permanent inmates of mental hospitals. Sexual activity may be possible, and female imbeciles often become prostitutes of the lowest class.

Both imbecility and idiocy are often combined with epilepsy, *i.e.*, the underlying brain condition gives rise to both mental deficiency and epileptic fits.

The diagnosis of a moron is more difficult, not so much in the distinction from imbecility (which is mainly a matter of nomenclature) but in the distinction from normality, especially " normal " stupidity. Once the idea has arisen, it is not, of course, difficult to carry out suitable tests. But it is surprising how rarely the physician thinks of this diagnosis if he sees the patient, not in a psychiatric out-patient department but in a general ward where he or she complains of peculiar sensations, or disturbs the other patients by behaving like a naughty or tiresome child. A considerable proportion of those who seem maddeningly incapable of giving a straightforward or consistent history are morons, and hypochondriacal reactions are very frequent amongst them.

Since the majority of morons live outside mental hospitals, this class is of much greater medical and social importance than the other two. The same

[1] For details of the whole question see: Burt, C., " Mental and Scholastic Tests," London, 1922. Terman, L. M., and Merril, M. A., " Measuring Intelligence," London, 1937.

variations of character are found among morons as in normal persons; but the intellectual defect, which is often coupled with poor powers of self-restraint or "inhibition," often provides the background for certain anomalies of character, especially aggressiveness, criminal propensities, and sexual libertinism. The make-up of the individual moron may influence even the test results by means of which the intellectual level has to be gauged. Lack of interest, and of concentration and effort, may bring the results below the "potential" intellectual level. Special disabilities, *e.g.*, in the field of speech, in reading, and in calculating, may have a similar effect.[1] Performance tests, used to supplement the Binet-Simon scale or other "verbal" tests, may be of great assistance in examination. Earl has shown that the relation between the "verbal" and "performance" scores is of special significance; morons with psychopathic propensities tend to do better in verbal tests, while good results in suitable performance tests point to a good social adaptability.

Feeble-minded persons contribute substantially to the number of criminals and prostitutes. Their fertility rate is higher than that of the average population, a point which has been largely used in the propaganda for sterilisation. It is, however, worth remembering that minor degrees of mental deficiency are fairly common in the lower social strata of the community, and that such persons are often useful members of the population not easily replaced in the performance of dull and simple tasks.

Ætiology of Mental Defect.—The causes of mental defect are so numerous and the type so varied that no really satisfactory classification is as yet possible. The genetic factor is of predominant importance in the majority of cases who are often classified as suffering from *primary amentia*, distinguished in principle, though it is frequently difficult to distinguish them in practice, from the smaller group of exogenous origin or the *secondary amentias* where there is evidence, or it is supposed, that the development of the brain has been arrested by some adverse factor in the environment, *e.g.*, birth injury or early cerebral disease.

Although there are certainly exceptions, when the Intelligence Quotient (*vide* p. 755) is below about 45 the probabilities are in favour of a secondary amentia. The high-grade defectives, corresponding more or less to the legal class of the feeble minded, should be regarded as very backward persons and, as in the case of stature, the mental defect to the extent that it is hereditary, has to be attributed to the cumulative effect of many genes. Low-grade mental deficiency embraces a number of different entities of different causation. Sometimes, as in *amaurotic family idiocy*, the condition is undoubtedly due to a single recessive gene, but in other instances, as in *mongolism*, although there is a hereditary basis, whether the potential mongol in fact develops, the condition depends upon non-genetic factors of whose nature we are ignorant. As has been indicated above, purely non-genetic influences, *e.g.*, birth trauma, may cause low-grade mental deficiency. Amongst the better recognised clinical types may be mentioned the *microcephalic idiots* where the skull is not only small in circumference (17 in. or less), but also has a characteristic shape with a receding forehead. Cretinism is often combined with a degree of mental deficiency. The results of thyroid

[1] "Idiot savants" are mental defectives who have exceptional abilities in a limited field; lightning calculators, memory prodigies, etc., have been described.

treatment in this condition, if started in early life, can be beneficial, the patients becoming more vivid although their intellectual state does not show similar improvement.

ORGANIC SYNDROMES

Organic syndromes are distinguished by two main criteria: (i) certain characteristic mental symptoms, and (ii) the ætiological preponderance of physical factors. These mental symptoms are known as organic mental symptoms, and it is most important to be familiar with them; for without this knowledge it is not possible to assess the importance of physical findings in mental disorder, or to reach a conclusion as to whether they are co-incidental or causal. Again, their presence should lead to the search for relevant physical factors that might otherwise have been overlooked.

Classification of Organic Syndromes.—It is convenient to make a necessarily rough division into those cases that are associated with permanent pathological changes in the brain and those which are not.

The former are known as organic dementias; by dementia is meant a deterioration of the personality predominantly in the intellectual sphere but also in the character. Impairment of memory and judgment, emotional lability, and deterioration of the finer feelings are the predominant features.

No single term has gained general acceptance to designate all the members of the second or potentially recoverable class. These can be divided according to their severity into (i) organic neurasthenia and (ii) delirium and allied states.

One syndrome may be present during the whole course of an organic psychosis, or the various types of reaction may alternate. All organic reaction types may lead to dementia, but this may develop insidiously without passing through any of the other stages. Finally, delirious reactions frequently occur in the course of a progressive dementia.

Organic Neurasthenia implies a state of fatigue and irritability often coupled with headache, hypochondriacal attitudes, and subjective complaints of memory disturbance and difficulty in concentration.

Mild cases never pass beyond such a condition; but the symptoms of organic neurasthenia are frequently seen both in the early stages and in the convalescence of the more severe reactions to be described below.

A similar picture to that of organic neurasthenia is often, however, seen, which does not result from the operation of organic causes (*vide* Anxiety States, p. 783).

Delirium and Allied States

These include delirium, clouded consciousness, and Korsakow psychoses. There is a clear need for a dictator in psychiatric nomenclature, for some of these conditions are also known as "exogenous psychoses," "infective exhaustion psychoses," "toxic confusional psychoses," and "symptomatic psychoses" by different authors in different countries.

Ætiology.—Except in the case of the mental changes that follow the administration of certain rare drugs, such as mescal, the mental symptoms produced by various intoxications, or different forms of physical disorder and disease, are not in themselves specific. Thus typhoid fever and pneumonia can produce the same mental picture,

The degree of mental disturbance, as well as its type, depends upon the constitution of the patient as well as upon the intensity and duration of the intoxication.

Clinical Picture of Delirium—(*a*) *Physical Symptoms.*—Apart from the accompaniments of the infection or intoxication in question, a sluggish reaction of the pupils, nystagmus, and diplopia are often found. Slurred speech and paraphasia are not uncommon, and evidence of inco-ordination is brought out by attempted movements. Bladder control is often defective.

(*b*) *Mental Symptoms.*—Important points are the following : (i) disorientation ; (ii) difficulty in grasp and impairment of memory ; (iii) increased suggestibility and responsiveness, together with a tendency to embroider or to "confabulate" ; (iv) hallucinations, especially visual hallucinations ; (v) paranoid features ; and (vi) restlessness or psychomotor activities variously elaborated. The lucidity of consciousness changes quickly : a patient may be deeply somnolent when left to himself, but give a few quick relevant answers when roused.

Variability in all the symptoms, which is constant unless the patient is so toxic as to be stuporous, is clearly bound up with the increased responsiveness, for these patients respond to all stimuli with abnormal facility and intensity. The increased suggestibility, with which is coupled the tendency to embroider or to elaborate, can often be shown when patients can be induced to read from blank sheets of paper, or when these patients give a circumstantial account, which is entirely untrue, of where they have been or what they have done. The same point is shown in the various misinterpretations. Every type of experience is liable to be misinterpreted. Thus the bed-cover may be thought to be a coat ; the doctor is mistaken for a relative ; or a sore tongue is attributed to malicious burning. These misinterpretations are in part dependent upon expectations and fears, and they frequently, as in the last instance, display paranoid tendencies. They are also dependent upon the difficulty in grasp and clouding of consciousness which, in some degree, is invariable. This constantly changes, but at all times attention is poorly sustained, concentration is difficult, and thought is laboured and often disconnected. These patients readily tire, are distracted by outside happenings, or sink back into the confusion from which they have been partially aroused. The memory for recent events is particularly poor, and in the more severe cases gross disorientation is shown.

Visual hallucinations are extremely common and are highly characteristic (*vide* p. 735). They can be terrifying and are most frequent in acute intoxications. Auditory hallucinations are less frequent, but may persist for a time after visual hallucinations and evidence of gross confusion have disappeared. A smaller number of patients complain of olfactory and tactile hallucinations. The hallucinations have frequently an illusional basis.

All the points that have been mentioned are clearly seen in the paranoid attitudes and delusional ideas, which are typically transient and ill-systematised, and which are, in part at least, dependent upon the difficulty in grasp ; for if difficulty is experienced in a clear grasp of what is taking place, it is comprehensible that doubt and suspicion should arise. Further, they are in part dependent upon the increased suggestibility. Misinterpretations are often the starting-point for delusional formations.

All delirious patients at some time and to some extent feel themselves the subjects of persecution or annoyance, which may range from vague ideas of

reference to more crystallised beliefs evidenced by talk of plots, gangs, wars, and revolutions. Others believe they are to be poisoned or killed or tortured, or that they are in danger and about to be robbed or kidnapped.

The degree of restlessness varies, and ranges from tremor to the most highly co-ordinated and purposive movements. Many toss and turn, grope, kick, and rub. "Investigating" and occupational activities are highly characteristic. These patients will search vaguely or indulge in activities familiar to them, such as driving their cars or telling their rosaries. Finally, as might be expected, the mood is commonly a dreamy, dazed, drifting state, very labile, and with rapid changes. Perplexity, irritability, mistrust, and definite suspicion are frequently seen. Anxiety may change into frank fear, and in many fear is the dominant affect throughout. Talk of suicide, or even definite suicidal attempts, are by no means uncommon. On the other hand, euphoric states and phases may be seen.

Delirium tremens is the term commonly applied to acute delirious reactions of alcoholic origin. They usually last between three and six days, and end suddenly, often with a long sleep. Though it is quite true that alcohol is the most common cause of acute delirious reactions with confusion, restlessness, fear, and vivid visual hallucinations as prominent features, yet the same picture may result from other intoxications. It is not therefore necessary to describe the symptoms of delirium tremens separately. The physical symptoms, namely, tremor, ataxia, tenderness of the nerve trunks, may lead to the correct diagnosis.

The dominant features of the delirious reaction can be summarised by the statement that it is a variable, restless, suggestible, confused, and clouded state with a striking frequency of visual hallucinations and paranoid tendencies and ideas accompanied by a labile mood predominantly irritable, anxious, fearful, and depressed. Such a general statement leaves out the individual personal setting and colouring which plays a large part in shaping the delirious reaction that is shown. This connection is more obvious if the disturbances are of relatively light intensity, for if the depth of the disturbance is too great, individual differences tend to become blurred. In the less severe disturbances manic or depressive features, or whatever it may be, may greatly colour and even appear to dominate the picture.

Prognosis.—The prognosis of a delirious state will of course necessarily depend mainly upon the physical disorder or disease responsible for the condition. Physical prostration consequent upon restlessness and excitement may, however, materially alter this course, and may induce a fatal issue which otherwise would not have taken place. Broadly speaking, the unstable and psychopathic, the young and the mentally defective, are particularly liable to develop delirious reactions of a wild and impulsive type.

In the vast majority of cases the prognosis as regards the mental state is excellent, and recovery is rapid and complete. There are, however, certain important exceptions. It is not uncommon to see delirious reactions resulting from alcohol or bromide superimposed upon other psychoses, and after the delirium has cleared up the underlying psychosis will then become evident and rapid recovery will not take place. A careful history should avoid this difficulty.

Again, delirious reactions may usher in a psychosis of an ominous variety which was not apparent prior to its onset. Certain schizophrenic and paranoid psychoses may start in this way.

It is always wise to be more guarded about the prognosis if the personality of the individual sufferer is such as to give grounds in general for psychiatric concern, especially when schizophrenic features are to be observed during the course of the illness itself.

Finally, a delirium occurring in those with organic brain disease may clear up, leaving an organic dementia of greater or less degree. Korsakow syndrome is a frequent sequel of alcoholic delirium.

Treatment.—Attention to the underlying physical cause of the condition is of course the first consideration, but a great deal can be done in other ways.

It must be remembered that these patients are unable to differentiate or discriminate, or to grasp situations that are new, complex, and unfamiliar. Thus, particularly in the case of elderly patients, removal to the strange atmosphere of a hospital ward may precipitate mental symptoms.

Conversely, quiet, simple, and familiar surroundings tend to prevent or ameliorate delirium, and it is most important to try to reduce the chances of misinterpretation to a minimum. Constant reassurance and explanation must be given, preferably by the same doctor or nurse, for these patients can be soothed and quietened nearly as readily as they can be upset and perplexed.

Simple Clouding of Consciousness.—In many cases a fully developed delirious reaction never occurs. During the day such patients may complain merely of feeling weak and tired, with difficulty in concentration, and examination may only disclose some mental dulling or slowness. During the night, however, and in the more severe cases during the day as well, definite confusion with transient disorientation and difficulty in grasp may become more obvious. With this are frequently coupled visual hallucinations, at first hypnogogic, or of the " elementary " or simple type that has been described (*vide* p. 735). In addition there may at times be evidence in various forms of the labile mood change described in classical delirium, as well as fleeting paranoid tendencies or ideas of reference. Restlessness and broken sleep may also be observed.

Bromide Intoxication.—These states of simple confusion are not uncommon in the less severe degrees of bromide intoxication : and when this is so, the diagnosis is frequently missed because of the predominance of the depressive or anxiety symptoms for which bromide has been ordered.

An apparent change for the worse in any " functional " syndrome taking the form of increased suspiciousness, nocturnal restlessness, and especially increased difficulty in grasp, should always raise the possibility of bromide intoxication ; and when tests for intellectual capacity (memory, calculations, etc.) reveal defects, these suspicions should be strengthened. The examination of the blood bromide will then clinch the matter. A blood bromide of 200 mg. per 100 c.c. is almost certain to be accompanied by symptoms of intoxication, but these may occur in specially susceptible persons at lower figures.

Korsakow or Amnesic Syndromes.—In this variety of organic reactions which, it is important to stress, although most frequently to be observed in, is not confined to, alcoholism, the memory disturbance is the most striking feature, and not the difficulty in grasp or clouding of consciousness. On the contrary, these patients may at first sight appear to be normally quick in the uptake ; and they often speak with great fluency and apparent plausibility. But examination reveals gross memory defects. These defects are most obvious in the appreciation of time relationships, especially for recent

events. In order to compensate, as it were, for these memory defects, these patients *confabulate*, and often show the most striking suggestibility, so that they tell the most extraordinary and inaccurate tales, amplifying them with full and quite fictitious details on little pressure. A lack of initiative and a fatuous or indolent mood are commonly seen. Polyneuritis, originally described as an essential feature (polyneuritic psychosis), may or may not be present.

A large proportion of the cases of amnesic syndromes develop out of a delirious state.

The prognosis of a fully developed Korsakow syndrome is poor, and the usual outcome is a silly, cheerful, but irritable condition with some disturbance of initiative and grasp.

The treatment of the alcoholic is always a matter of the greatest difficulty, and it has been said that the effect of treatment is often merely to render the patient sufficiently fit to start drinking again. As regards breaking the habit, deconditioning methods, which consist in forcing the patient to drink alcohol and giving him at the same time some emetic drug with the hopes of establishing an aversion, in skilled hands seem to be less unsatisfactory than other methods. This treatment has the additional advantage of being relatively quick.

THE ORGANIC DEMENTIAS

All organic dementias have many features in common, and the main characteristics have already been given. They resemble the potentially recoverable organic syndromes in that the clinical pictures also seem to be mainly referable to the intensity of action and duration of operation of the morbid process, and to be at least relatively independent of the exact nature of this process.

The possible variations in the clinical picture and course will best be appreciated by considering them under some of the more common causes responsible for their production. It must be appreciated that the various morbid processes to be described, though they tend to produce permanent pathological changes in the brain, do not always do so, with the result that the degree and type of dementia, and the possibilities of partial or complete recovery or remission, vary.

General Paralysis of the Insane

In this section only the mental symptoms are dealt with. Other features of the disease, including the results of malarial treatment, are dealt with elsewhere (*vide* pp. 639 and 646). The cardinal symptom is a progressive deterioration of the personality, both in intelligence and in character; depression, excitement, stupor, and disturbances of consciousness can be regarded as accessory symptoms which may or may not be present. The onset is usually gradual; and even when the disease appears to start suddenly or dramatically, with a state of confusion or fit, a careful history will generally reveal the presence of symptoms of an organic neurasthenia previously: these include headache, fatiguability, slight complaints or evidence of memory failure, and reduced resistance to alcohol. Some change in behaviour may have been observed by relations or friends who knew the patient intimately.

Thus it is common to hear that patients have been more irritable, more egotistic, and less considerate than formerly; that they ate, talked, and drank more than was their previous wont, and showed less sexual restraint. Objective evidence of memory impairment, especially for recent events, names, and dates, may have been evident, and the patients may have become more careless and their writing less tidy and correct. In spite of these early symptoms the patients may be able to deal with their work well enough, especially if it is of a simple or routine nature. But they often fail when called upon to show any special initiative or judgment, or when faced with any exceptional or difficult task. This may lead to the belief that the stress imposed by the particular situation has led to the breakdown, which is thought to be of a so-called functional type, and hence diagnostic mistakes may be made unless a careful history is taken and a thorough examination carried out for organic signs.

With the progress of the illness the patient becomes more indolent and apathetic. Depression, when it occurs, is superficial. Hypochondriacal and melancholic ideas are often silly and inconsistent. Disturbances of memory are prominent features, and even when immediate retention (*vide* p. 733) is not so bad, recollection and reproduction of recent material is often grossly at fault. This is apparently due to the combined effects of disturbances of attention, of the capacity to synthesise, and of remembering in the more strict sense; and other factors that contribute are the disturbances of judgment that interfere with the patient's capacity to criticise and correct his own wrong answers, especially when this is combined with a lack of interest.

The final stage of the illness is characterised by a profound and generalised dementia. The defects of memory grow, until even old and familiar material, such as the dates of birthday, and of marriage, and even the names of children, disappear. The patient fabricates spontaneously, or can be induced to do so. The disturbance of memory and judgment finally becomes most profound. One patient threw his cigar butt out of an upper window, and wanted to follow it through the window to have another puff; and another patient, with optic atrophy, constantly forgot his blindness and asked for the lights to be turned on.

The most contradictory statements can be made and accepted. The mood varies between apathy and euphoria, and the characteristic emotional lability is generally evident. Hand in hand with the mental deterioration goes a progressive physical deterioration leading finally to an extreme degree of wasting and paralysis.

The course of the disease and the clinical picture may differ considerably from that which has been described. There is an acute type, rapidly progressive, often with numerous fits and a very bad prognosis. The expansive or classical form, which is nowadays rare, is characterised by a demented euphoria and ideas or delusions of grandeur. ("He, he, he," said one patient when asked to multiply five by two, "you can't catch me; ten million.")

Depressive symptoms in the depressive form may disguise the dementia, although the melancholic or hypochondriacal ideas usually lack coherence and system. Catatonic and paranoid pictures may occur in the course of the illness, the latter with relative frequency during or immediately after malarial treatment.

Juvenile paralysis develops as the result of congenital instead of acquired

syphilis. There is a progressive intellectual deterioration, with the usual neurological accompaniments. The picture is even less dramatic than the simple demented form of the adult type, and the prognosis is bad.

Mental Symptoms with Vascular Disease

The mental symptoms that occur with hypertension, whatever its pathology may be, can be distinguished from those that result from arteriosclerosis, though possible transitions and variations must be borne in mind.

The presence of either hypertension or arteriosclerosis often facilitates the production of other types of reaction of so-called functional type ; thus the presence of the symptoms of anxiety or depression may, and not infrequently do, so dominate the picture that organic factors and organic mental symptoms may be overlooked. Similarly hysterical reactions are often " released."

The preliminary stage of either type of cerebral vascular disease shows the non-specific but characteristic picture of organic neurasthenia : increased irritability and fatiguability, headache, insomnia, subjective disturbances of memory, and frequently giddiness. The irritability is often associated with a tendency to become easily " flustered " (organic lability of mood).

Hypertension.—Short attacks of interruption of consciousness, very similar to petit mal, may occur. What might be regarded as an extension of the same phenomenon, namely, confusional states of variable duration and with varying features, may also call for psychiatric treatment. Such attacks may follow an apoplectic seizure ; but in other cases no neurological signs can be discovered on which the assumption of structural damage to the brain can be based. During these confusional psychoses, the blood pressure may be either higher or more fluctuating than it was before.

The clinical picture may be that of delirium, and, especially when the patient is an alcoholic subject, an acute delirium. In other cases, depressive or, more rarely, manic pictures with confusional features dominate the picture ; and finally ecstatic states can be observed.

Prognosis.—The normal duration of these attacks is a few weeks to a few months, but in some cases the psychosis only lasts a few days.

The confusions that so frequently occur at night in arteriosclerotic and senile patients may well be of the same nature.

The prognosis for these states in themselves is good ; but there is always the danger that the emotional disturbance and concomitant rise in blood pressure may precipitate a cerebral hæmorrhage.

Recovery, when it takes place, is usually complete, but repeated attacks usually leave behind residual symptoms, often at first very slight. In the long run essential hypertension, with or without acute episodes, and with or without apoplectic strokes and subsequent focal symptoms, is liable to bring about an alteration of personality. These patients become irritable, difficult to get on with, forgetful, narrow in their outlook, labile in their emotions, and less dependable in every respect. Their intelligence is, however, very slightly impaired, and they usually retain very good insight. This, coupled with their emotional lability, tends to increased self-observation and worry about their condition, with secondary bad results on the blood pressure.

Treatment.—This vicious circle should be the object of psychiatric

treatment; and even the hypertension itself may respond well to suitable psychological management and psychotherapy.

Arteriosclerosis.—In arteriosclerotics the neurasthenic syndrome of the prodromal stage blends into that of a slowly progressive dementia. Arteriosclerotic deterioration differs from the intellectual deterioration produced by other causes, especially general paralysis of the insane, in that arteriosclerotic deterioration is more patchy and less generalised. The façade of the patient's personality is preserved longer and more completely. For a considerable time what might be called the peripheral functions of intelligence are impaired rather than the " central " functions of judgment, reasoning, and insight.

Thus the patient may show marked impairment when examined by the usual tests for memory, but be able to keep his end up, and to conceal his defect from the outer world with the aid of a notebook or diary and a strict routine, though he may have to struggle very hard.

The disturbance of the finer feelings that is so conspicuous in early general paralysis of the insane is absent in the early stage of arteriosclerosis, but as the illness progresses it becomes more apparent. The patients develop, together with an increased emotional lability, a gradual deterioration of their higher feelings and social instincts. They become increasingly egotistic, and feel less warmly about their friends and relations. Sexual activity may reappear as the result of impaired inhibition; and, owing to the lack of opportunity or capacity for normal satisfaction, the patient may finally fall back on infantile forms of gratification, such as exposure and obscene practices with children. These patients are often referred to the psychiatrist by the courts.

Insomnia is a characteristic symptom of the early stages, and may finally lead to, or be combined with, the motor restlessness and slight confusion that develops as the disease advances. The patients become exhausted by their nocturnal restlessness and sleep half the day. They may damage themselves during these periods of restless confusion at night either by falling when they try to get out of bed, or by stumbling in their disorientated state in the darkened room.

The picture is often complicated by focal symptoms due to cerebral thrombosis.

The *Differential Diagnosis* from early general paralysis of the insane and cerebro-vascular syphilis is the main problem. Though the types of dementia show some characteristic differences already described, serological examinations of the blood and cerebrospinal fluid must be performed. A slow-growing cerebral tumour may produce a similar mental picture.

Prognosis.—The ultimate prognosis in cerebral arteriosclerosis is bad, but it is difficult to predict the rate of deterioration.

Treatment.—The treatment is that of arteriosclerosis in general (see p. 430). The psychiatric therapy is purely symptomatic.

Senile Dementia

Senile dementia may be looked upon as an exaggeration of the usual psychological changes of old age. It is a progressive deterioration in which disturbances of memory are conspicuous. It is normal for people in their old age to become more narrow in their outlook and rigid in their views. Senile

patients show these points in exaggerated form or even in caricature. In addition, they have difficulty in grasp. The combination of these factors leads to increased distrust and suspicion, and provides the basis for the numerous paranoid features of the senile. The disturbances of memory and of judgment prevent these ideas from being developed into a real delusional system ; but ideas of reference and of persecution are very common. The senile patient often complains that everything is stolen from him ; and such ideas are favoured by greediness and forgetfulness.

The patients become increasingly egotistic and their emotional life becomes shallow ; the deaths of near relatives make little impression. In contrast to the emotional poverty, emotional expression may be increased (organic lability). Decrease of potency and loss of control account for sexual offences, such as lewd practices with little girls. A person committing such an offence for the first time in old age should always be examined by a psychiatrist. Senile dementia is often not recognised in its earliest stages by the layman.

The interest and initiative shown by the senile decrease often rapidly ; but sometimes they develop an empty restlessness, especially in the evening and at night. They then totter about aimlessly, more or less confused, start to get up, to pack, or try to leave the room or house.

Presbyophrenia.—This is generally described as a particular type of senile dementia, and is characterised by a very gross memory impairment for recent events, coupled with an unusually well-preserved personality. These patients are generally pyknic in build and possessors of a hypomanic temperament.

The physical symptoms are those of old age. Tremor, an impassive expression, and an increase in muscle tone are often seen. Gross focal symptoms are evidence of superimposed vascular disease and do not belong to the typical picture.

The Morbid Anatomy of senile dementia shows histological changes apart from the general signs of senile involution of the brain that are not, however, entirely specific. They need not be gone into here.

The Prognosis for senile dementia is, naturally, very bad as regards recovery ; the prognosis as regards life depends upon the physical state of the patient. Much restlessness and confusion tend to shorten the course owing to physical complications.

Presenile Dementias.—Whereas the usual age for hypertensive disease is between forty-five and fifty-five, for arteriosclerosis between fifty-five and seventy, senile dementia rarely begins before the seventieth year of life. But there is a group of cases where a slowly progressive dementia, similar to senile dementia, is observed earlier in life, beginning in the fifties. Amongst others, the following types have been described :—

1. *Alzheimer's Disease.*—There are certain features that make the diagnosis of Alzheimer's disease possible, even apart from the age of onset. The dementia is very profound, but the behaviour of the patient and the emotional responses are surprisingly well preserved. Symptoms of aphasia, agnosia, etc., are also frequent, but less well defined than when they result from focal lesions of vascular origin. Stereotyped movements and speech are very common, the latter finally deteriorating into repetitive utterances that are meaningless.

2. *Pick's Disease* is somewhat similar in its clinical picture, but differs

in pathology. Circumscribed areas of atrophy can be found in the frontal or temporal lobes, or both. This disease is sometime familial.

The clinical picture in the early stage often resembles that of general paralysis of the insane. Death occurs after six to twelve years.

3. *Huntington's Chorea* is often given as a third type of presenile dementia (see p. 613). The dementia has no particular features ; changes in character sometimes precede impairment of memory and judgment, and both may be evident before the chorea develops.

Mental Symptoms in Encephalitis Lethargica

The mental symptoms during the acute phase show nothing exceptional or particularly characteristic. After recovery from this phase the patients are often inert, restless, and slow, and the development of Parkinsonism is generally preceded by a neurasthenic picture, the patients being described as irritable, moody, and hypochondriacal. The Parkinsonian state is generally accompanied by a slowing down of all psychic processes and is not associated with a true dementia. But this general slowing is combined with loss of initiative which may give rise to a picture that resembles a dementia, and which certainly results in the reduction of the level of the previous personality ; yet tests demonstrate that all the fundamental mental faculties are well preserved. Sometimes schizophrenic or paranoid pictures develop, and the obsessional and compulsive phenomena that occur during the oculogyric crises are of great theoretical interest. The patients report that during these crises they feel impelled to say or to do something. They may also show obsessional symptoms between the attacks.

Encephalitis lethargica occurring in childhood may result in a peculiar picture and produce a very gross change in personality. After the acute phase children may become increasingly restless, irritable, and aggressive, and appear to lose all moral sense. They beg, steal, lie, and are cruel to other children and to animals. They talk incessantly, cling to those they meet and cannot be detached, and become unmanageable at school and at home. Abnormal sexual curiosity and sexual problems are also often observed. Even in milder cases lack of concentration interferes with any successful work at school or subsequently.

Post-encephalitic adolescents sometimes show certain features of the above syndrome, especially a lack of sexual restraint.

The prognosis of post-encephalitic conditions in children was originally regarded as very bad, but follow-up studies show that about one-third become socially adaptable in spite of organic brain disease ; another third develop Parkinsonism.

Mental Symptoms in Epilepsy

Epileptics are often subject to periodic changes of mood, characterised by surliness and irritability. Such periods may or may not precede epileptic attacks.

Epileptic psychoses usually follow an epileptic attack, but they may also occur independently. In the first instance, the patients do not recover consciousness as usual, but remain in a clouded state, disorientated, confused,

slow in grasp, and tending to perseverate, They often appear tense and perplexed, and are sometimes restless. They may wander about, and are often arrested by the police because they are behaving in a strange manner. It is this type of patient who may be seen suddenly undressing in the street or exposing himself. In other cases this picture of simple dimming of consciousness is complicated by hallucinations and motor excitement, giving rise to the picture of an epileptic twilight state. The hallucinations are unusually vivid, and great fear is a very prominent feature. Sometimes a religious ecstatic mood and a corresponding content prevail.

Epileptics in twilight states are the most dangerous patients. They defend themselves against their supposed attackers, or attack those about them. They refuse any sort of treatment, struggle wildly, and may attempt suicide. Patients with recurring twilight states always seem to act in a very similar way. These twilight states seldom last longer than a fortnight, and no means of cutting them short is known. Close supervision is necessary, and treatment by some form of continuous narcosis is often adopted. Some patients respond to luminal by the development of these twilight states and this should be borne in mind when deciding on treatment.

At least two-thirds of all epileptics show progressive deterioration of variable degree, and there is some correlation between this deterioration and the number of fits. The psychological picture of epileptic deterioration can be regarded as an attenuated form of the post-paroxysmal confusional reaction. Patients become slow, have fewer ideas and associations, and tend to express themselves in an increasingly circumstantial manner. Their mental horizon narrows, and they lose interest in all except themselves and their illness. "My fits" become their favourite topic, and there is often an interesting contrast between this increased concern and their optimistic attitude towards their disease. They tend to believe that their fits have now ceased or their number is decreasing or their severity is less. This makes it difficult to judge the result of treatment without observation in hospital. Epileptics are often outwardly submissive and polite in their peculiar circumstantial way. Many of them turn to religion and become over-devout and bigoted ; but it is the devoutness of religiosity, and fundamentally they are sensitive, irritable, suspicious, and egotistic. If there are several epileptics in the same ward they usually quarrel. The epileptic disturbance of memory is mainly, especially in the early stages, a difficulty of recollection, another expression of their poverty of association. It is therefore noticeable both for remote and for recent material.

Mental Symptoms following Head Injury

Concussion is a state of unconsciousness or disturbed consciousness produced by a sudden mechanical injury to the brain. It is more frequently seen in closed than in open injuries, and does not necessarily occur in penetrating injuries such as gunshot wounds. The disturbance of consciousness may vary from simple dimming of short duration to complete unconsciousness lasting for hours or days. During recovery from the latter the patient passes through the stages of dimming of consciousness as described on page 729. Subsequent amnesia and retrograde amnesia are discussed on page 734. Neurasthenic symptoms, especially headaches (of an organic character), may exist for a considerable length of time after a concussion.

In severe concussion and cerebral contusion, recovery from unconsciousness is protracted and various complications may arise. The patients may remain slow in grasp, with little initiative and with more or less severe disturbances of remembering with or without the tendency to confabulate; or they may become restless, excitable, and actively delirious. They are often extremely cheerful, and have surprisingly little insight into their condition, even after the acute phase of delirium has passed. The recovery is gradual; a state of depersonalisation may be observed in the transitional stage.

A confusional state may sometimes be observed as the result of cerebral compression, occurring instead of unconsciousness, but possessing the same diagnostic significance.

The prognosis for post-traumatic psychoses depends on the type, degree, and extent of the brain injury and on the general physical condition of the patient. Arteriosclerotic and alcoholic patients are less likely to recover as quickly and as completely as do young and vigorous patients. Severe post-traumatic psychoses not uncommonly last as long as three months, and in a proportion of cases the recovery from delirium or an amnesic syndrome is followed by a neurasthenic condition.

Focal symptoms sometimes point to localised damage to the brain, and poverty of motor activity with euphoria and lack of insight may be signs of local injury to the frontal lobe. The lack of insight is often not recognised as a morbid symptom at all.

When symptoms persist after damage to the brain they have the general characteristics of dementia, in which sometimes intellectual impairment and sometimes a change of character predominate. Traumatic epilepsy may in severe cases lead to a progressive epileptic dementia.

In a small number of cases psychoses of manic-depressive or, more frequently, of schizophrenic type follow head injuries; the more closely they are related to the accident, the better the prognosis.

Differential Diagnosis.—After head injuries, as after other accidents, mental symptoms may develop that are not due to the injury to the brain but to the emotional shock and to the subsequent distress consequent upon the physical injury, or altered circumstances arising indirectly from the accident. The so-called shock neuroses are rare after serious head injuries, probably owing to the subsequent amnesia for the accident itself. Far more common are hysterical reactions (*vide* p. 785). But when examining a post-concussional case with neurotic symptoms it should be borne in mind that the type of response shown by a patient can be altered by damage to his brain; all patients, and especially those who give no history of previous hysterical symptoms or hysterical predisposition, should therefore be examined most carefully for organic mental symptoms; organic lability of affect and disturbances of concentration and memory will often be disclosed by a thorough examination, or from a careful history obtained from an independent source. Standardised psychological tests of deterioration (Babcock, Shipley) are a valuable help in the diagnosis, but they require careful interpretation in the light of all other data. Many changes in behaviour following a head injury are not necessarily due to structural damage to the brain and consequent change in the patient's personality, but are caused by psychological factors often only loosely connected with the event that caused the accident.

SCHIZOPHRENIA

(*Dementia Præcox*)

The term "schizophrenia" ("split mind"), first proposed by Bleuler to describe what he held to be the cardinal feature, is now substituted for the older term "dementia præcox," which gives an unfortunate and misleading impression; for there is complete agreement that the onset in these psychoses need not necessarily be early (præcox) nor result in a dementia.

It is now believed that "paranoid states" or "systematised delusional insanities," which are sometimes described separately, should really be regarded as belonging to the schizophrenic group, which is hence sometimes described as the "schizophrenic paranoid series."

The discussion on the definition and delimitation of the schizophrenias is not yet closed. Difficulties arise because some writers use the term schizophrenia as the name of a disease (characterised by certain cardinal symptoms, its course, and a hypothetical pathological "process"). Here it is applied to a clinical syndrome independent of cause, course, and possible pathology. Confusion may be avoided if a distinction is made between schizophrenic symptoms and a series of schizophrenic illnesses.

Clinical Picture.—The clinical symptoms in the different types of schizophrenia are so numerous and varied that it is proposed to describe them first, and to deal later with their relative diagnostic values and their grouping in different syndromes and types.

Emotional Disturbances.—Irritability and oversensitiveness may be early symptoms, but shallowness or poverty of emotional response, together with a general apathy and loss of interest in the outside world, are more characteristic. Loss of emotional rapport may often be felt by the observer or by the friends and relations before it becomes clearly manifest in the patient's behaviour. Yet the patient may feel it himself and complain of it, or he may experience it as a change in the outside world. In more advanced cases the loss of emotional response is often disguised behind a silly, cheerful indifference. Schizophrenic incongruity and inadequacy of affect (*vide* p. 733) are often clearly seen in these more advanced cases, and this may make the patient's emotional response appear incomprehensible to others. Finally, the indifference and emotional impoverishment play an important part in leading to dirtiness, self-neglect, self-exposure, and shameless masturbation.

Disturbances of *emotional expression* are closely related to, and are often difficult to distinguish from, inadequate and incongruous emotions. Giggling for no apparent reason, or for an apparently inadequate reason, is often an early anomaly; and in later stages, quite apart from its appropriateness, the expression of emotion may be unusual in itself, stiff, or slow and bizarre, so that the patient's behaviour resembles bad acting.

The emotional deterioration leads to a progressive withdrawal of these patients from contact with the outer world, so that they become more and more solitary, self-absorbed, and frequently hypochondriacal, until finally they appear to live entirely in a world of their own.

Disturbances of Volition are often combined with the emotional disturbances. The patient may himself complain of lack of energy before the friends and relatives notice the poverty of initiative, and the lack of decision

and determination. In the later stages these may become so profound as to leave the patient an immobile figure sitting or standing about in the wards of a mental hospital. But when the disturbance is less severe, patients of this type are frequently found either sitting about at home, or amongst the vagabonds who drift about the world without aim or purpose.

The severest form of this disturbance constitutes stupor, which may be combined with abnormal suggestibility shown in its extreme degree in the so-called automatic obedience (*vide* p. 780).

Ambivalence is the term used for another characteristic schizophrenic feature : contradictory impulses are present simultaneously, or arise in rapid succession. This is often well seen when such patients are asked to shake hands. Thus the patient may begin to hold out his hand and then withdraw it ; the examiner then withdraws his hand ; whereupon the patient holds his hand out again, only to withdraw it once more when the examiner makes a response. When a request or suggestion is immediately followed by counter-impulses the disturbance is called *negativism*.

Disturbances of Motor Activity.—The same incongruity may be observed in the various types of schizophrenic activity. A state of apathy may be interrupted by the performance of some sudden impulsive action, so that these patients may suddenly start shouting for no apparent reason, become destructive, or attack others. These sudden outbursts of activity are sometimes carried out in obedience to hallucinatory voices, but in other instances patients who are able and willing to provide information are often unable to give any reason for them.

States of more prolonged excitement are also common ; the patients may indulge in strange attitudes, or show peculiar movements, apparently expressive of such states as terror or ecstasy, or they perform wild and purposeless, apparently incomprehensible, movements. The movements themselves are often not performed with the normal degree of precision and co-ordination. Stereotyped repetitions are often seen, such as rocking, knocking, and rubbing. These anomalies of motor activity are often included in a group of symptoms that are called *catatonic* (automatic obedience, echo actions, stereotypy).

If flexibilitas cerea is combined with automatic obedience, the picture of catalepsy results (*vide* p. 730).

In mild cases a lack of gracefulness may be an early sign ; and in more advanced cases the movements may become peculiarly stiff and clumsy and finally result, owing to the addition of tic-like movements and distortions and alterations of the normal tempo, in the so-called mannerisms, which make the whole behaviour appear very eccentric and bizarre. Slight mannerisms may be left as a residual symptom after recovery.

Some patients are very well aware of their disturbance of volition ; but in many instances it is projected and rationalised, so that the patients come to believe that others interfere with their decisions and actions, and that their will is under some outside control (passivity feelings). The primary disturbances of volition may be variously elaborated and systematised into delusional ideas according to the strength of the paranoid tendencies. Many catatonic phenomena are explained by patients as due to the actions of voices.

Thought Disorder.—A poverty of ideas and associations may be all that is noticeable at first, but a sense of sudden interruption or blocking in the stream of thought is more characteristic.

The most important disturbances of thought are seen in the schizophrenic association of ideas. In well advanced cases this becomes evident in the spontaneous utterances, which sound incoherent or entirely incomprehensible, but in milder cases it may only come to light if the patient is given a set problem, or as the result of association tests.

The thought disorder cannot be reduced to a single mechanism, but some of the components, such as condensation and displacement of ideas, as well as a tendency to symbolic thinking, may be discerned. These all resemble dream mechanisms. Hence schizophrenic thinking has been compared with the type of thinking which many normal people experience immediately before they go off to sleep, or when asleep.

The schizophrenic thought disturbance may result in "double orientation." Thus a patient may believe he is God or the King, and may act and speak accordingly. But at the same time he may act and speak as an inmate of a mental hospital and will argue with the doctor and complain about the other patients.

These two lines of thought may be kept up in spite of all contradiction; or they may be interwoven. There is no logic, or the logic is peculiar.

From the subjective point of view schizophrenic patients may, in the early stages, complain of difficulty in concentration. Many such patients turn their attention to subjects that lend themselves to vague speculations such as mysticism and spiritualism, and so-called philosophy and psychology; and this is often interpreted as an over-compensation for their vaguely felt incapacity. But when the thought disorder becomes worse, the patients usually lose insight gradually. The thought disorder colours the various delusional systems, and is one of the main constituents of the so-called schizophrenic dementia.

The elements of language may be well preserved, but various mutilations of individual words may occur, so that the verbal production of these patients may resemble that of an aphasic. In the most severe stages, language is disintegrated into a sequence of incomprehensible syllables and neologisms (word salad).

Early cases often show an inclination for highbrow, odd, or artificial expressions (mannerisms of speech). Newly coined words or neologisms usually result from the patient's urge to describe his experiences, for which purpose an ordinary vocabulary is inadequate.

Hallucinations of any of the senses may be found; but auditory hallucinations are the most frequent and characteristic (*vide* p. 736). Their clarity varies. Some patients are able to describe the character of the voices in great detail, and the impression may be so vivid that the patient answers hallucinatory questions and discusses the statements of his supposed interlocutors. Other patients, although they are immediately aware of what the voices say, cannot repeat the exact words or otherwise describe the sensory character of their experience. The voices are generally disagreeable, threatening, aggressive, and abusive, and frequently make allusions to sexual matters. Sometimes the voices give orders that are often carried out to the letter, and hence it is always important to determine what hallucinatory orders are received.

The most characteristic type of schizophrenic hallucination occurs when the patient hears his own thoughts repeated, either immediately before he has conceived them, or simultaneously with the process of thinking, or

immediately afterwards. In later stages the voices become more incoherent and incomprehensible, and neologisms often appear.

Visual hallucinations are rare (*vide* p. 735). Sometimes patients complain that small pictures flash through their visual field, or that the objects they see look distorted, or that the vividness or quality of what they see has changed.

Hallucinations of taste and smell are often woven into the delusional ideas, in the production of which tactile or other physical sensations also play an important part.

Hypochondriacal self-concern is a very important and frequent aspect of the patient's introversion. Paræsthesiæ and various pains may be described in detail, and the peculiar sensations are often described at first with the help of strange metaphors : thus, feelings as if the body were twisted or as if the testes were galvanised. But soon the descriptions lose their " as if " character, and the patients then say that their bodies are twisted and that they are galvanised. These hallucinations gradually blend into hypochondriacal delusions, which typically have a very bizarre character.

Schizophrenics very commonly complain of feeling influenced by rays, or complicated physical devices, or of being the victims of all kinds of lewd practices.

The hallucinations lead to all manner of explanatory delusions ; but the characteristic schizophrenic delusions are known as " autochthonous " delusional ideas (*vide* p. 732). These " primary delusions " are elaborated, explanations added, and the whole starting point of the delusional system may be subsequently forgotten. The degree of systematisation and elaboration of the schizophrenic delusions depend to a large extent on the severity of the coexisting thought disorder. Ideas of reference and delusions of persecution are the ones most commonly found, in addition to hypochondriacal delusions. Thus patients come to believe that others are against them, that their relatives, the police, or the Jews persecute them, until finally everybody is involved in the plot. The passivity feelings (*vide* p. 731) are usually given a paranoid twist, and all the delusional ideas are often confirmed by the hallucinatory experiences. Delusions of grandeur may coexist with the paranoid delusions, but they may also exist independently. Thus the patients often believe they are persecuted because they are the possessors of remarkable powers, or because they are the Messiah. Erotic aspirations towards those of superior social status are frequently seen.

Misinterpretations of the most varied kinds, such as of the pictures or advertisements seen in the newspapers, are often quoted to confirm the delusional system.

Although for practical purposes it is much more important to distinguish the clinical types, the following entirely schematic classification may be useful in remembering the main symptoms :

1. Symptoms of Withdrawal : Introversion, hypochondriasis—emotional and habit deterioration—stupor.
2. Symptoms of Splitting : Double orientation—ambivalence—thought disturbances and incongruity of affect—impulsive actions.
3. Paranoid Symptoms : Projection—hallucinations—delusions.

Clinical Types of Schizophrenia.—Three groups are commonly recognised : (1) Simple—hebephrenic, (2) Catatonic, (3) Paranoid—paraphrenic.

1. *Dementia Simplex—Hebephrenic Group.*—Dramatic symptoms are characteristically absent in the early stages of this type, which usually begins in late puberty. The patient shows a falling off of interest and initiative, and the decreasing capacity for adaptation to ordinary life may be disguised in hypochondriacal complaints. Sometimes the hebephrenic process seems to stop at this stage, leaving behind an odd, dry, withdrawn, egocentric hypochondriacal personality as a defect. In other cases the patients show an increasingly poor work record, tend to neglect themselves in their personal appearance, and friction arises with other members of the family for no apparent reason. The patients lose their self-criticism and self-control, and become very exacting or even brutal. This behaviour may be difficult to distinguish from the churlishness of adolescence, but usually occurs beyond the age when a reaction of puberty would be a justifiable explanation. With the progress of the illness the withdrawal from reality becomes more marked, the hypochondriasis increases and becomes more bizarre, evidence of thought disorder becomes noticeable, the emotional response becomes more shallow, slightly paranoid ideas and finally hallucinations may develop. These symptoms are often masked by a fatuous euphoria or indifference.

In other cases the onset is more acute, and the picture of a depressive or an anxiety state may be the first evidence of illness. But after some months hebephrenic deterioration becomes manifest.

2. *Catatonic Group.*—These psychoses begin somewhat later, the majority between the ages of twenty and thirty-five. There is generally an acute onset, and the clinical picture is either that of a stupor or of a state of excitement. The motor symptoms that have been described dominate the picture, and the tendency to sudden impulsive actions makes those patients most dangerous to themselves and those around them. The psychosis may start with an acute state of anxiety or perplexity, with an abundance of hallucinations and autochthonous delusions. Certain cases of catatonic excitement show manic features which may make the diagnosis from manic-depressive psychoses difficult without prolonged observation.

Catatonic psychoses usually subside, but the completeness of the recovery varies, and the type and degree of the residual defect cannot be foretold until the acute symptoms have faded. Recovery may appear to be complete and may last for a considerable period, but ultimately a recurrence usually takes place either in the same form, or in a less acute type of schizophrenia. Recurrent catatonia is a rather characteristic type. Deterioration generally becomes manifest after the second or third attack, as shown by a shallowness of emotion, thought disturbance, or some form of social inadequacy.

3. *Paranoid Group.*—These psychoses are the latest in onset, the majority of them starting in the fourth decade. They develop insidiously. Sensitivity and suspicion gradually develop into paranoid ideas, and the development of hallucinations completes the picture. The delusions are not generally systematised, and various delusions often coexist without being related or combined. The discrepancy between the grotesque delusions, the terrifying hallucinations and the poor emotional response which they evoke, is often very striking, and this may enable the patient to have some insight into his condition. Thus he may complain: "I am suffering from ideas of persecution": and a German paranoid schizophrenic wrote to his physician during the war: "I have been given the Iron Cross. The schizophrenic indifference is appreciated in the front line."

The name *paraphrenic* has been given to those sufferers from paranoid psychoses who, in spite of numerous hallucinations and more or less systematised delusional ideas, yet retain their personality in a relatively intact state. Thus the patient may show few symptoms of withdrawal or thought disorder, and the emotional rapport may remain strikingly good. Paraphrenic psychoses begin later in life than the other paranoid psychoses, often at the time of the climacteric or the beginning of the involutional period. The preservation of the personality may be due either to the fact that the pre-psychotic personality was of a resistant type, or to the late onset, or to both.

Paranoia is now regarded as a still milder form of paranoid schizophrenia, and the picture is that of a well elaborated delusional system in a personality that is otherwise well preserved. Hallucinations are absent, but falsifications of memory to fit the patient's past into his delusional system are very common. The classical picture is very rare, and takes a very chronic course.

Some paranoiacs live in liberty as queer inventors, founders of eccentric sects, or as social reformers ; but the majority are ultimately admitted to mental hospitals because of some friction with society.

These clinical pictures represent well-known types, but they are not separate entities. When a case is observed for a sufficient length of time combinations and permutations can usually be observed : catatonic outbursts in simple hebephrenic or paranoid states ; paranoid developments in hebephrenia ; and hebephrenic deterioration after a catatonic psychosis. Observations of this kind provide the decisive argument for the close relationship between all the different clinical types of schizophrenia.

Physical Findings and Pathology.—Cyanosis of the extremities, evidence of endocrine dysfunction and various abnormalities of the physical structure, are common in all types of schizophrenia. The closest association, however, seems to be between the asthenic habitus and hebephrenic psychoses.

Degeneration of the cells of the testis has been described in a large proportion of schizophrenics, but no other characteristic anatomical findings have been confirmed.

Biochemical abnormalities are equally elusive, except that it would appear that a disturbance of nitrogen excretion accompanies certain well-defined recurrent cases of stupor and catatonic excitement, which enabled Gjessing not only to predict the onset of subsequent attacks, but also to abort them by the administration of thyroxin to increase the nitrogen excretion.

Ætiology.—Schizophrenia is a hereditary disease. This is borne out by its comparative frequency in relatives of manifest schizophrenics. Kallmann found the following rates of expectation. Of the children of one schizophrenic parent, 16·4 per cent. become schizophrenic ; if both parents are schizophrenic, 68·1 per cent. ; amongst siblings, 11·5 per cent. ; amongst half-siblings, 7·6 per cent. ; whilst in the general population the incidence is about ·85 per cent. The exact nature of inheritance is still controversial, Kallmann assuming a single factorial autosomal probably recessive transmission, whilst other authorities favour a gene with incomplete dominance. What might be called the penetrative power of the hereditary factor is below 100 per cent., since, if one of a pair of uniovular twins is schizophrenic, only 65 to 80 per cent. of the partners develop a manifest illness.

Diagnosis and Differential Diagnosis.—The most striking symptoms of schizophrenia do not always possess the highest diagnostic value. Thought

disorder and shallowness of emotional response rank first ; autochthonous delusional ideas are extremely characteristic ; whereas other kinds of delusions, hallucinations, and catatonic symptoms are frequent in many other conditions. Yet delusional ideas of a bizarre character, passivity feelings, and especially the complaint by a patient that he hears his own thoughts, are rarely encountered in non-schizophrenic psychoses. So much for the diagnosis from the examination of the patient.

The history and prolonged observation is generally decisive. In order to establish the diagnosis of a progressive schizophrenic illness it is necessary to discover whether the personality of the patient has changed, and if so, whether this change is schizophrenic in character and whether it may or may not be due to environmental or developmental factors. The more extroverted the pre-morbid personality of the patient, the more noticeable will be a change towards introversion, seclusion, and emotional shallowness. On the other hand it may be impossible to recognise with certainty minor changes in this direction in a schizoid, sensitive, shy, shut-in type of personality. In such patients it may be difficult or impossible to distinguish mild depressions or neurotic reactions from an early schizophrenia.

The presenting symptoms of a recent schizophrenia may closely resemble those of a state of anxiety, depression, or panic ; and the diagnosis may only be permitted or suggested with the development of additional symptoms, especially hallucinations and autochthonous delusions.

The diagnosis of a catatonic from a manic excitement is easy in clear-cut cases. But manic features may be present in catatonic states, and then the diagnosis may depend upon the presence or absence of cardinal schizophrenic symptoms. Isolated catatonic features, however, such as stereotypy and grimacing, within a manic picture, must not be regarded as decisive evidence for the diagnosis of schizophrenia. Catatonic symptoms may also result from vascular brain disease. In such cases the discovery of organic signs will decide the diagnosis.

Toxic confusional states may produce pictures very similar to schizophrenic psychoses, but clouding of consciousness is then a marked feature, whereas it occurs only rarely and transiently in the acute form of schizophrenia.

Prognosis.—The prognosis of the average case coming under treatment is very serious. It is possible that the outlook is more favourable for mild cases which do not come under psychiatric observation. Follow-up studies, conducted ten to twenty years after the first outbreak, show that about two-thirds to three-quarters of the patients are either dead or permanent inmates of mental hospitals. Even after a period as short as three to four years 40 to 50 per cent. are social invalids. After such a period about one-third of the patients can be regarded, for all practical purposes, as cured ; the remainder are either improved, though not fully recovered, or run a periodic course, with relapses and remissions. About 35 per cent. of the cases recover or show a considerable improvement after the first attack.

The prognosis in an individual case is a matter of great difficulty. An old rule, which still holds good, is that the more acute the onset, the better the prospect of a remission. If the onset is insidious, as is usual in cases of hebephrenia, the prognosis is bad. For acute catatonic states the prognosis is more hopeful, though the possible physical complications of both excitement and stupor (exhaustion, physical damage, aspiration pneumonia) must

be remembered. Paranoid pictures tend to progress, but social adaptation may be possible in spite of the continuance of the symptoms.

The patient's age is of importance only so far as it predisposes to particular types of psychoses. A pre-psychotic personality of schizoid type reacts unfavourably on the outlook, as does a schizophrenic heredity, whereas manic-depressive psychoses in the family may point to a remittent course. The prognosis for patients of a pyknic build is more favourable than for those of asthenic physique, or for those who show signs of endocrine dysfunction.

Treatment.—As regards treatment, the patients may be divided into two classes; those in and those outside mental hospitals. Again, in mental hospitals, the acute and chronic cases require different treatment. For advice as to general management, reference may be made to the general section on treatment, page 742. Chronic cases benefit most by occupational therapy. Wherever this is carried out by up-to-date methods, the mute and stiff catatonics who were previously so common are not to be seen. With carefully thought out treatment and management it is possible to bring these patients back to some sort of community life.

The treatment of schizophrenia of recent origin has been revolutionised by the introduction of shock therapy, and the outlook for many chronic cases has been greatly changed by the introduction of prefrontal leucotomy. The assessment of the results of new methods of treatment in schizophrenia is extremely difficult because of the great variation in the spontaneous remission rate. There is now good evidence, however, that insulin treatment leads to more frequent, better, and more lasting remissions than occur either spontaneously or with the aid of E.C.T. alone, the latter form of treatment being increasingly regarded as only effecting symptomatic improvement, for example when affective complications cloud the picture or in cutting short a stuporous or excited phase. It may be concluded that a full course of insulin shock treatment should always be given in cases of recent origin and should be considered even in chronic cases. The workers emphasise that insulin treatment must be combined with psychotherapy and management of the patient's daily life, and many workers find that a mixture of insulin with E.C.T. is the most effective method. Insulin shock treatment consists in producing a series of hypoglycæmic states and interrupting them after varying periods by the administration of glucose; the intensity of the hypoglycæmia is gradually increased up to deep coma. The treatment is given on six days a week; not less than thirty comas should ever be given and it is seldom effective to go beyond sixty. As has previously been mentioned, prefrontal leucotomy has been performed with undoubted success in noisy, aggressive, and destructive schizophrenics, and reports are now coming in of many chronic cases who have not responded to other methods of treatment but who have been able to leave hospital and adapt themselves with varying degrees of success in the external world after the operation.

Early cases, without acute symptoms necessitating admission to a mental hospital, may benefit from environmental treatment, such as change of surroundings and removal of factors which tend to produce sensitivity, hypochondriacal or paranoid ideas. In more advanced cases of the hebephrenic type, and in cases of schizophrenic defect, the main object of treatment is the patient's readjustment to social life. Nothing gives such relief to a patient as freeing him from the stress of an occupation which he can no longer manage and putting him to a simple task in which he may once more become a useful

member of the community. The longer an attack lasts beyond six months the less likely is recovery.

THE AFFECTIVE SYNDROMES

The increase in knowledge that has taken place during recent years no longer permits of the clearly cut division between manic-depressive psychoses, other forms of depression, and neuroses, that was formerly deemed to be possible. It must be realised that, although it is necessary for teaching and classification to describe the affective reactions under various headings, transitional and mixed states not only can be found but occur frequently.

Manic-depressive States

According to the classical definition put forward by Kraepelin, manic-depressive psychosis is a mental illness characterised by emotional fluctuations and concomitant disturbances of will and thought. Though the prognosis is good and there is no residual mental defect, there is, however, a marked tendency to relapse. Manic and depressive psychoses are grouped together because : (i) they may alternate in the same case, (ii) some of the striking symptoms may be regarded as exact opposites. The symptoms of manic-depressive psychoses are both physical and mental and are given in tabular form below :—

Depressive States.	*Manic States.*
1. Sadness.	1. Elation.
2. Motor retardation up to stupor.	2. Hyperactivity.
3. Retarded thinking.	3. Flight of ideas.
4. Delusions of self-reproach, depersonalisation, hypochondriasis.	4. Delusions of grandeur, mental and physical.
5. Suicidal ideas.	5. Aggression.
6. Loss of sexual desire.	6. Increased sexual desire.
7. Sallow complexion.	7. Ruddy complexion.

Loss of weight, constipation, insomnia and, frequently, amenorrhœa are found both in manic and depressive states.

Within the manic-depressive psychoses various types may be distinguished :—

1. Depression with retardation : classical melancholia which, in its most severe forms, passes into depressive stupor.

2. Hypomania and mania.

3. Depression without retardation : mixed states with anxiety, agitation, and hypochondriacal and paranoid features. All these features are common in involutional melancholia.

The Depressive phase of manic-depressive psychoses (melancholia) usually begins and ends gradually. The cardinal symptom is the depressive mood. The patient feels sad or listless and apathetic. Anxiety is frequently combined with the depression and the patient complains of pressure in the head, precordial sensations, and a sense of oppression in the chest or abdomen.

The melancholic mood colours the whole outlook on life—past, present, and future—pessimistically. The patients worry about their economic

condition and their own prospects, as well as those of their wives and children. They tend to turn their fears into facts, so that they may come to believe that they are financially ruined, or that their families are starving, sick, or even dead. This may go on to nihilistic ideas that they are themselves dead and that the world does not exist. But these nihilistic ideas may also originate from the hypochondriacal preoccupations that are very common in melancholics. They complain that their organs do not work, that their stomach cannot digest food, that their bowels are blocked, that their heart does not beat, that their genital organs are decayed. Sometimes, instead of feeling that they themselves are changed (depersonalisation), the outer world appears different (derealisation). In depersonalisation the patient feels different from what he used to be, strange, lifeless, detached, automatic. In derealisation the outer world looks dead or macabre. In " affective loss " the patient complains of loss of feeling, often given a self-reproachful twist, *e.g.*, he feels " hard hearted." All transitions and variations may be found.

Melancholic patients are inclined to blame themselves for their condition, and feelings of guilt and self-reproach are most characteristic features. The patient looks into his past and there finds causes for regret and self-reproach. Falsifications of memory on these lines are not infrequent. The self-reproachful ideas generally follow the popular views of moral and medical causation, and thus the illness is attributed to masturbation, or lack of consideration and love, or some other " sin," real or imaginary.

Paranoid delusions often develop from the self-reproach, so that the melancholic comes to believe others look at him, and indicate his unworthiness by word, look, or gesture. Hallucinations are exceptional, but illusions and misinterpretations frequently occur. The paranoid ideas are consistent with the mood and appear comprehensible in the light of the patient's attitude and outlook. Obsessional features are often present, even when the patient had none before the illness.

Suicide.—Every melancholic patient must be regarded as a suicidal risk, and many patients are admitted to hospital after suicidal attempts. These patients may plan suicide carefully and dissimulate their intentions. Whilst in hospital, strangling, hanging, and jumping out of the window are the favourite methods ; at home patients frequently try to gas themselves or to swallow poisons. The morbid fear for the future of their dependants sometimes leads to well-intentioned homicide before a suicidal attempt, and this may lead to an especially tragic situation if the shock of the homicide prevents the intention of suicide being carried into effect. Suicide would probably be more frequent in melancholic patients were it not that another cardinal symptom, *retardation* (*vide* p. 731), has a somewhat antagonistic effect.

The retardation may only be noticeable to the patients themselves, who find that every thought, word, movement, or decision requires a greater effort than normally. If, however, retardation becomes more marked, the slowness may become apparent to the outside observer. In the most severe form a condition of melancholic stupor results.

Retardation cannot be regarded as the simple accompaniment of the depressive mood, for the retardation and depression may vary independently of one another, and not infrequently retardation improves before the depression. This explains why the risk of suicide is specially great during the period of recovery, even greater than at the height of the illness. Again, retardation may be more marked than the depressive effect throughout the illness, and

it is generally regarded as possessing greater diagnostic significance in so far as the endogenous type of depression is concerned. The intensity of the symptoms may vary with or without an obvious external cause. It is very common for depressions to be worse in the morning and to improve somewhat towards the evening. This morning and evening variation is often connected with the disturbance of sleep, but many patients complain of feeling worse after a good night.

The insomnia of depression is characteristic in that the difficulty is not so much in going off to sleep as in waking up early. Sexual desire is diminished or absent, and impotence is frequent, even in the early stages, which may lead to hypochondriacal and self-reproachful elaboration. Loss of weight is another very constant feature, and although the loss of appetite usually leads to reduced intake, it can be shown that this does not wholly account for it.

Other physical findings are of less importance. The blood pressure tends to be somewhat higher than is normal for the individual, and nearly all depressives complain of constipation.

Mild forms of melancholia may be disguised as "organ neuroses," *i.e.*, vague complaints of indigestion, constipation, and precordial sensations may be the most conspicuous symptoms. Closer investigation may disclose insomnia, and a certain amount of retardation with or without manifest depression. A history of previous phases of mania or depression may be elicited.

Mania.—In many respects the symptoms of mania may be regarded as the exact opposites of the symptoms of melancholia. The dominating effect is elation, and the patients are gay, cheerful, and feel better than ever before. But they are often irritable as well, and this may be one of the most prominent features throughout. Sleeplessness and irritability are often the first symptoms. These emotional symptoms are coupled with overactivity. The patients start to do more, undertake larger enterprises, and indulge in greater risks. The increasing number of these new enterprises soon makes it difficult for any one to be completed. In severe cases activity becomes disconnected and purposeless. Impulses follow one another in rapid succession, and the manic patient can brook no interference or restriction and becomes aggressive and violent. At the height of manic excitement, consciousness may be dimmed and the patient may become completely exhausted. Flight of ideas as opposed to retardation is the characteristic disturbance, and the patients talk, shout, or sing incessantly. Jokes and rhymes, accompanied by vivid and expressive movements, are poured forth. Manic patients are very distractible and weave everything they see or hear into their utterances. Grandiose ideas may be developed, but are usually put forward in a jocular vein. Some make hypochondriacal complaints, but utter them with manic vigour. Hallucinations are rare, and if present, are in keeping with the grandiose ideas and the elated mood. The increased sexual desire and lack of inhibition may result in all sorts of difficulties. Manics may for a time present the picture of perfect health, but soon signs of exhaustion and starvation become evident.

Hypomania shows the same symptoms as mania, but to a lesser degree. It is therefore more difficult to recognise, and it is often most difficult to convince a lay person or a judge that the cheerfulness, overactivity, lack of control, and argumentative irritability are evidence of a morbid condition.

Manic-depressive states do not always conform to the classical picture that has just been described.

It is most important to bear in mind the possibility of *minor attacks*, and a carefully taken history will often reveal mild phases of depression or elation that were never regarded as illnesses at all.

Again, the symptoms may appear in different combinations to those seen in classical melancholia and mania. The existence of these intermediate or mixed forms is shown very convincingly in *manic stupor*. In this extremely rare condition patients may exhibit a most striking lack of manifest activity; but after recovery they describe their euphoria and flight of ideas which they were unable to express owing to their extreme motor retardation.

Depressions without retardation or even with excitement (*agitated melancholia*) can also be regarded as examples of mixed forms which, however, have great practical importance because of their frequency. They are most commonly seen in the involutional period, but can also occur at a younger age. These patients are tense, anxious, and fearful rather than sad, and the corresponding affects colour or dominate the clinical picture, which can be that of extreme restlessness and agitation with much sobbing, wringing of hands, and incessant complaint and lamentation. Owing to their lack of retardation they can be dangerously suicidal.

An absence of retardation is also often regarded as one of the most characteristic features of *exogenous* depression, but the difference between *exogenous* and *endogenous* depressions on this point—as in all other respects—is one only of degree. The symptoms in a typical exogenous depression follow immediately upon some event which makes the reaction comprehensible in the light of the patient's personality and circumstances, the abnormality of the emotional reaction consisting in its duration and intensity. Throughout the illness the patient is only concerned with this causative event or situation and its possible consequences. Thus he will brood over how it came about or might have been prevented, blaming himself or, more typically, others for sins of omission and commission. Finally, an improvement in, or adaptation to, external circumstances tends to lead to a more rapid recovery than is seen in endogenous conditions.

Few patients fulfil all these criteria for an exogenous depression, and the number is further reduced if the latent fallacy of a "spurious psychogenesis" (*vide* p. 723) is clearly recognised.

Involutional depression is often diagnosed (*a*) if the illness starts about the involutional period, and (*b*) if the patient has never previously suffered from a manic or depressive phase. The main features are agitated depression with much apprehension and anxiety, hypochondriacal ideas, often of a bizarre character, a preoccupation with the theme of death, and various paranoid reactions and paranoid delusional formations. The usual depressive delusions may be present as well. Exactly the same clinical picture may, however, occur in manic-depressive states at this time of life, in which the original personality is probably an important determinant.

Course.—Cases of classical recurrent type usually start between the twenty-fifth and fortieth year. Depressive states are more frequent than manic, and in more than two-thirds the first attack is a depression. Two-thirds of the cases recover completely; the rest swing over into the opposite phase before recovery. A considerable number have only one clear-cut

attack. It is impossible to predict what intervals will elapse between attacks in those that have recurrent illnesses. The duration of individual attacks varies enormously. As a rule they last between six and eight months, but attacks of two or three weeks' duration may occur, as well as those that last two or three years. In the interval, the patients appear well, although mild hypomanic features may be noticed by relations after depressive illness, or some moroseness after a manic state. After several attacks, such alternations in mood may be observed more frequently, and it is then sometimes difficult to judge whether these patients suffer from a series of minor mood fluctuations or from a definite change of personality.

The Prognosis.—For the individual attack the prognosis is good, but recurrence is probable. Advanced age, arteriosclerotic features, or atypical (schizophrenic) psychoses in the family are all points that should lead to greater prognostic reserve. Retardation is the symptom which has the highest correlation with a good prognosis.

The prognosis is always more serious if the first attack occurs at the involutional period. The duration of an involutional depression is often given as between nine and twelve months, but many cases last a much longer time. As has been pointed out, the course and duration of an exogenous (neurotic) depression are more closely related to the event or situation which was responsible for its production. It must, however, be remembered that both manic and melancholic states of endogenous type may be precipitated by emotional shock or stress, and the subsequent illness may last as long as did previous attacks which were not so precipitated. The characteristic feature of these endogenous illnesses, precipitated by psychological factors, is that the content tends to lose connection with the precipitating event. These points must, however, be taken as guiding principles rather than as rigid rules, for even in the most endogenous cases the content of the depression must necessarily be determined to a considerable extent by the patient's past experience and circumstances ; and even when a depression appears psychologically comprehensible as a reaction to some external event, the type of the patient's response is largely affected by constitutional factors. It is therefore necessary to study each case individually before the relative importance of constitutional and environmental factors, and their bearing on the prognosis, can be assessed.

Ætiology.—The constitutional factors are demonstrated in the heredity, in the pre-morbid personality, and in the patient's physique.

For reasons previously put forward, genetic studies are particularly difficult to make in psychiatry ; but those having their origin in indubitable cases of manic depressive psychoses suggest that the condition is probably due to a single dominant gene although only 20 to 30 per cent. of the carriers develop the illness. Figures recording the liability of the various relations to be affected are 9·5 per cent. for the children and 2·5 per cent. for the nephews, nieces, and first cousins, the figures for the general population being given as between 0·2 and 0·4 per cent.

Manic-depressive psychoses are much more frequent in women than in men. The climacteric is an important precipitating factor. A certain number of cases develop after childbirth. It is now recognised that there is no specific puerperal insanity, and breakdowns occurring at this time may be of any type. It is not rare to hear from patients that they were always liable to mild depressions at the time of their menstrual periods. In other cases the

onset occurs after severe infections, especially influenza. Manic-depressive psychoses are quite frequently precipitated by strokes, and this lends some colour to the belief that severe head injuries may be important as well. There is little doubt that the psychological situations arising out of accidents—mutilation, prolonged hospitalisation, loss of employment—may cause depressions, but hysterical elements often predominate in such cases. The importance of psychological factors and experiences has already been mentioned.

Differential Diagnosis.—The differential diagnosis between the various types of depression can be limited to the assessment of the relative importance of endogenous and environmental factors. Hysterical and obsessional features are not inconsistent with the diagnosis of depression, but they are of great importance for the prognosis in the individual case. Affective pictures may disguise the early stages of schizophrenia. Retardation and schizophrenic anergia must be carefully distinguished. Hypochondriacal and paranoid ideas, if in keeping with the affective state, also do not preclude the diagnosis, but if they become bizarre or incomprehensible in the light of the prevailing mood, they point to a schizophrenic illness. Again, shallowness of affect should arouse the suspicion of schizophrenia. Demonstrative statements of being depressed may be part of an hysterical reaction. Depressive pictures also occur in organic conditions such as general paralysis. High blood pressure, or evidence of arterial thickening, should suggest the possible role of vascular disease, but organic dementia is often difficult to demonstrate if retardation dominates the picture. Manic states must be distinguished from catatonic excitement; a euphoric mood, contact with the surroundings, and distractibility are in favour of the former diagnosis; whereas stereotypy, mannerisms, and negativism speak for schizophrenia. As with depressive pictures, the possibility of organic conditions, such as general paralysis, must be borne in mind.

Treatment.—Any physical factors must, of course, be dealt with in so far as this is possible. The management, psychological treatment, and psychotherapy in general have been dealt with elsewhere (*vide* p. 742). All depressive patients require reassurance, and mild cases usually respond well to it. As a general rule it can be said that the more reactive the case the more is psychotherapy indicated; that includes a thorough psychological investigation of the patient's problems and their reformulation with a view to helping in his readjustment.

As mentioned previously (*vide* p. 744), E.C.T. can be said to have revolutionised the treatment of manic-depressive psychoses. The main indications appear to be depressions of endogenous type or with endogenous features, and particularly good results are obtained in the older age groups. Although it is true the majority of depressions recover spontaneously within a reasonable period, the results obtained with E.C.T. are so good that it should always be considered and should usually be given in depressive states unless the history suggests that the illness is likely to be short-lived. Quite apart from the months of illness and misery that may be avoided, the danger of secondary symptom-formation and elaboration can also be reduced. The results with manic states are on the whole less satisfactory, and fewer of such illnesses appear to be cut short although they may be made much easier to manage. E.C.T. has been discussed previously (*vide* p. 744) but it may be well to record here that perhaps the best cases for treatment are those who show

diurnal variation coupled with indecision and the biological concomitants of depression, particularly disturbances of sleep. In practice a frequent combination is to combine E.C.T. with modified insulin therapy. Previous mention has also been made of prefrontal leucotomy (*vide* p. 744), and as indicated there most gratifying results can be obtained in chronic depressive states with tension who have not responded satisfactorily to E.C.T.

Anxiety States

Anxiety is a symptom which may occur in any psychiatric syndrome. In some affective reactions, however, the anxiety syndrome occurs in more or less pure culture. The ambiguous term "anxiety hysteria" is better avoided altogether. Anxiety, if used as a psychiatric term, denotes a condition of fear not clearly focused on any special object, accompanied by striking physical signs similar to those produced by the secretion or increased output of adrenaline, such as dilation of the pupils, rapid pulse, palpitations, rise in blood pressure, sweating, pallor, and tremor. The patients may complain of these physical effects when they intrude upon consciousness, or of other sensations more or less closely connected with what may be called the "adrenaline syndrome": dryness of the mouth, feelings of choking or suffocation, sighing, restlessness, fatigue, weakness in the limbs, feelings of fainting, frequency of micturition or of other sensations due to a more or less general vegetative upset. The sensations of suffocation may induce overbreathing, which may in its turn lead to the symptoms of hyperventilation tetany, such as tingling in the fingers and toes, muscular spasm, and finally some blurring of consciousness. The symptoms of an anxiety state are often, of course, further increased by self-observation and misinterpretation, leading to the development of a vicious circle.

Anxiety may occur in acute attacks, the first of which can often be traced back to some special experience. Subsequent attacks may then be provoked by any happening which comes to be associated with the original trauma; more and more events come to be so associated, so that finally the "conditioned reflex" is set going by some very slight stimulus with no obvious connection at all. This episodic or recurrent type of anxiety merges into the chronic anxiety state where the same symptoms, though generally milder in degree and varying in intensity, continue for long periods. Sufferers from episodic or recurring types of anxiety are seldom completely free from symptoms in the intervals between their attacks, but are irritable, tense, dissatisfied, and unhappy.

The term "anxiety state" should not be applied too loosely to any case that shows the symptoms. This mistake is often made, so that a large number of conditions are included that should be dealt with separately. Thus, as has already been mentioned, anxiety may be the predominant affect in depressive or schizophrenic illnesses. Again, patients who suffer from phobias, as the result of which they fear to do something lest anxiety may supervene, are better described under the heading of "obsessional neuroses," to which they are clinically related by other features. Finally, anxiety states and their physical accompaniments may be intensified or prolonged by psychological mechanisms of an hysterical type, involving some secondary gain, *i.e.*, the wish to escape from some difficult situation. Thus anxiety states can, and often do, blend into hysterical reactions, just as do certain physical illnesses,

as when organic paralyses are complicated or prolonged by hysterical developments and mechanisms. The term "organ neuroses" is often used when the main symptomatic emphasis is concentration upon some one or other of the physical accompaniments of anxiety. It must, however, be stressed that not all "organ neuroses" are of this type. Some may be regarded quite simply as abnormal "conditioned reflexes," others are clearly hysterical from the start, either because they express some emotion metaphorically, or because they serve some personal purpose. Anxiety symptoms are only biologically and not personally purposive. The choice of the particular organ affected may be determined psychologically; but more commonly there is a constitutional factor in the choice. The physiological accompaniments vary from person to person, as does the response to adrenaline. It is probable that, of all the "organ neuroses," the cardiac neuroses bear the closest relationship to anxiety states, for the accelerated or forceful action of the heart is peculiarly prone to make a striking impression upon the patient's mind. As he is often inclined to "repress" the real cause of his anxiety, he readily finds his way to the heart specialist to whom is often left not only the differential diagnosis but the treatment of these states. In the same way it is probable that the striking physical accompaniments of sexual excitement account for the ready conversion of psychological disturbance in the sex life into the symptoms of anxiety.

Ætiology. — The physical accompaniments of anxiety have been experienced by nearly everybody. Although the threshold varies, the symptoms of an acute attack of anxiety can be produced in the most normal individual when a sufficiently large dose of adrenaline, caffeine, benzedrine or some similar drug is injected. The development of the symptoms of anxiety is therefore a potentiality which we all possess, and this may explain why anxiety states should be the most common of all the neurotic reactions and the least dependent upon the constitutional background. It is important to bear in mind the general principles of psychiatric ætiology which were outlined on page 721. As regards psychogenesis, the psycho-analytical school has proffered the formula "morbid anxiety means unsatisfied love." That this can be the correct explanation in certain cases need not be doubted; but it is generally held that this formula is too narrow, and that any conflict endangering the moral or social standards of the individual can result in the production of anxiety states. The war neuroses have demonstrated this on a large scale. The sufferers are usually unaware of the true nature of their conflicts or at least do not face them openly. They hence tend to turn their attention to their less vital problems, namely, their symptoms. This indicates the line of *treatment* that should be adopted. The patient has to be led to realise the shifting of emphasis that has taken place. The reassurance that "there is nothing *organically* wrong with him" is necessary; but this only constitutes the first step. The patient has to be led to realise the true basis of his difficulties and to readjust his standards to the requirements of his social environment in so far as the latter cannot be adjusted by him or for him. In the treatment of the individual anxiety attack the importance of the physical factors suggests an approach from the physical side. Drug treatment is indicated not only on theoretical grounds but also because of its success in practice. Bromides and hypnotics are of great benefit to the patient, and may indeed be necessary to tide him over the acute stage in which he will not be accessible to psychotherapy. In the severe cases of terror and panic as

observed during the war, continuous narcosis has proved to be the most efficient method for this purpose.

Hysterical Reactions

The term "hysteria" or "hysterical" is very ambiguous and often loosely applied in clinical usage and literature. It is commonly confused with the conception of "psychogenic," or, in other words, is employed to denote everything that is psychological in origin. It should, however, be restricted to those psychogenic reactions which are kept going for the sake of some gain which the illness brings, in solving some problem, or in fulfilling some wish, or in satisfying some desire in reality or in phantasy. In brief, it should be restricted to those psychogenic reactions which serve some personal purpose. This definition excludes such symptoms of psychological origin which are merely exaggerated accompaniments or metaphorical expressions of normal or abnormal emotions. The conception of psychogenic is therefore a wider one than that of hysterical, and includes such reactions as vomiting as an expression of disgust. This need not be hysterical, but becomes so if it is used for such a purpose as getting rid of a pregnancy. The patient is never clearly aware of this motive. The amount of repression that is seen in hysterical reactions varies greatly, and all transitions between hysterical reactions and frank malingering occur. It would, however, be a mistake to suppose that frank malingering is at all common, for, as has been rightly said, this would be a naïve underestimate of the capacity of human beings to believe what they think is in their own interest.

Ætiology.—Hysterical symptoms usually develop on the basis of some predisposition, constitutional or acquired. The predisposition may be greatly increased by experiences, especially the experiences of early life. Hysterical reactions are more common in women than in men, puberty is a favourite period, and emotional immaturity is often a striking feature of hysterical patients. The secondary sexual characteristics are frequently underdeveloped. Abnormal suggestibility on the mental side and lability of the vegetative system on the physical side are characteristic findings. Together they are probably responsible for the readiness with which hysterics convert psychological into physical symptoms. This "conversion" is a normal psychophysiological happening; we know, however, very little about the actual mechanism.

The hysterical personality has been described on page 752. The symptoms of an hysterical illness may be either physical or mental, or both. Physical symptoms may imitate those of almost any type of illness. Hysterical blindness, deafness, loss of cutaneous sensation, paralyses, spasms, tremors, are some of the usual gross manifestations, the differential diagnosis of which will be found in the description of the corresponding physical diseases. But the hysterical imitation of an illness is generally a very rough one, since it corresponds to the idea that the patient has of the symptoms of the illness. Thus hysterical anæsthesias are generally of the glove and stocking type, *i.e.*, they are limited to what the patients think is a functional unit. With the spread of medical knowledge among the general population, gross physical manifestations tend to decrease at the expense of vaguer and subtler complaints, such as headaches, giddiness, or feelings of faintness. Patients as a rule adopt a characteristic attitude towards their symptoms, either putting

up with them with the classical "*belle indifférence*," or demonstrating them ostentatiously. There are all transitions between trembling, shaking, and twitching, and the hysterical fit, the manifestations of which may be greatly changed by external circumstances, another aspect of the increased suggestibility. Thus the typical stages described by Charcot were certainly an artefact of the Salpetrière atmosphere. The motor phenomena often utilise physiological mechanisms, and it is therefore often difficult to distinguish between hysterical and extra-pyramidal symptoms, such as choreiform movements. In other instances the fit starts by overbreathing, and is coloured by phenomena due to the disturbed acid-base balance, such as clouding of consciousness and tetany, or kindred symptoms. Simple vasomotor collapse (fainting), though not hysterical in itself, may be used within an hysterical neurosis. The distinction between the hysterical and epileptic fit is discussed on page 652.

The mental manifestations of hysteria are twilight states, trances, fugues, and hysterical amnesia. The frequent utilisation of anxiety symptoms as part of an hysterical reaction has already been stressed.

Hysterical twilight states (often called Ganser) are mainly observed in prisons. They consist of a mild disturbance of consciousness and the symptoms are such as a lay person imagines a lunatic to show. Answers to all questions are so beside the point, or wrong in such a way, as to give a clear indication that the correct answer must exist somewhere in the patient's mind. Sometimes the condition passes into hysterical stupor, which may be difficult to distinguish from catatonic stupors, though generally vital functions are not so involved as in the latter condition. The discovery of situations which the patients had to face, but which they try to evade, may be helpful in the diagnosis, but it must be remembered that catatonic psychoses may also be precipitated by imprisonment, or the mental stress of the legal procedure.

A *trance* is a dream-like state which may be produced by suggestion or by emotional shock. Physical factors may assist in its production, as when small doses of hypnotics are given to make the patient drowsy, or after hyperventilation which normally produces a mild alteration of consciousness. The mechanism for the production of trance may be facilitated by practice, and some mediums readily pass into this condition. During trance, so-called automatic actions may be carried out, sensory perception may be altered, and hallucinations may be experienced. There is often a very vague recollection afterwards, or there may be a complete amnesia.

The term *hysterical fugue* is used for patients who wander whilst in such states ; they may be found far from their own homes, not knowing who they are or how they got there. Adequate reasons for such disappearances can usually be discovered.

Pathogenesis.—Many theories have been put forward to explain the mechanism of the hysterical reactions, some psychological, some physical, and some a mixture of both. It must be assumed that the physical symptoms have a physiological basis, and some of the physical mechanisms at work can be demonstrated. Yet a psychological factor is always necessary to set these physical mechanisms going, and in hysterical reactions there is always a flight into illness, or a defence mechanism with the object of gaining security or justification, that is not fully obvious to the patient.

A satisfactory and general solution of the problem as to how psychological

factors become converted into physical symptoms is as impossible as an explanation of the relationship between mind and body. The symptoms may be explained as the results of suggestion, but for this a condition of increased suggestibility must be assumed; or the reactions may be regarded as analogous to conditioned reflexes that are ground in by repeated elicitation. According to psycho-analytical views, the symptoms are due to affective energy originally belonging to some repressed material, and the symptoms produced express symbolically the repressed wishes or their gratification. It should be borne in mind that a medical examination increases suggestibility, and that hysterical manifestations are not infrequently the direct result of medical mismanagement. In particular, cutaneous anæsthesia and visual field defects are often artefacts due to the suggestive influence of an (unskilled) medical examination.

Prognosis.—The prognosis of the individual hysterical reaction is good, but the prognosis for the hysterical disposition is more serious and more difficult to assess. The disproportion between the stimulus and the reaction in the present illness or in previous illnesses, should these have occurred, may be used as a guide. Patients who have broken down in response to a negligible stress are more likely to relapse than those who are defeated by a severe strain. When frequent hysterical reactions have been shown, the outlook for the future becomes worse, and a marked hysterical character (*vide* p. 752) makes the prognosis more grave. Hysterical reactions in childhood or adolescence are less serious. Individual attacks yield more readily to adequate treatment, and the predisposition towards an hysterical response may be influenced from the environmental side, and very often diminishes or disappears after puberty.

Differential diagnosis of hysterical symptoms of a physical kind may be very difficult, especially when an organic lesion existed originally which is exaggerated or prolonged by hysterical mechanisms. The distinction between hysterical and epileptic fits has been discussed on page 652. Hysterical tics, tremors, and twitchings may be very similar to choreic or to extra-pyramidal syndromes. The influence of emotions and suggestions on the symptoms must be observed carefully, and a sound knowledge of neurology is necessary. The greatest difficulties are met with, however, in those cases with organic lesions that recover where the loss of function is maintained by hysterical mechanisms, as is frequently seen in disseminated sclerosis.

Treatment.—Hysterical mechanisms are a field for suggestive therapy of every kind, but the symptoms are likely to recur in the same or in a different form unless an attack is made on the basic psychological problems, or unless the environmental stress diminishes. It is therefore necessary to analyse the difficulties that have been experienced in the adaptation to life, and it should be remembered that hysterical qualities may be of value in the patient's readaptation. Many hysterics do very well in positions where they may play-act, or duly come in for self-demonstration or sacrifice, or where work permits them to find such attachments as they were previously unable to form.

War neuroses and *compensation neuroses* are special examples of hysterical reaction. In the former instance the wish to stay away from the fighting Services, and in the latter the attempt to obtain or to keep compensation, clearly provide reasons why the morbid symptoms remain. The symptoms of these neuroses are the same as those found in other hysterical conditions.

but are often much less dramatic in presentation, and may be mixed with those of an anxiety state. Fugues and amnesias have been found to be relatively frequent types of reaction in this war, and usually respond well to narco-analysis so far as the removal of the symptoms is concerned. Compensation neuroses seldom improve while any uncertainty as to the compensation remains, and if they do not improve after that, a thorough investigation of the patient's life becomes necessary, and readaptation according to the result of this should be attempted, aided by suggestive treatment for the particular symptoms that are shown.

Psychosomatic Medicine

The justification for this term would seem to lie in the production of previously somewhat neglected if not new methods of approach to general medical problems, these methods being essentially psychological. There are at least four different methods of approach that are called psychosomatic:

1. *Study of the psychological origin of somatic symptoms and of organ neuroses.*—As has frequently been emphasised, somatic symptoms are often the main and may be the only manifestations of a psychiatric syndrome. Such cases are usually seen initially by general physicians and not by psychiatrists. In this connection the student may find a brief summary of the differential points between affective and hysterical syndromes of value, since the majority of organ neuroses are dependent upon either one or the other or both combined.

Symptoms in the affective group are evidence of a psychosomatic reaction of the whole organism in a way in which hysterical symptoms are not. Thus subjective physical findings such as loss of weight and tachycardia may be observed. It may of course be argued that these physical concomitants of emotional disturbance are *biologically* purposive; but in purely affective states they are not *personally* purposive and are in no way desired by the patient, either consciously or subconsciously. Again, affective symptoms are not of the type that can be produced by voluntary effort. They acquire a certain autonomy of their own and are persistent. Finally, they cannot be abruptly terminated by changes in the environment. In brief, purely affective symptoms are impersonal symptoms outside the patient's control, although the patient can to a certain extent control his attitude to them and the degree to which he lets them influence his activity. In contrast, the symptoms in hysteria are not such as occur as the involuntary concomitants of emotional disturbance. They are more of a type that can be imitated by voluntary effort, they are not so persistent, and they are very much more modifiable by environmental changes and measures. These symptoms are not in any sense impersonal, and any change in the attitude of the patient is reflected in them at once; hence their fluctuation in intensity according as to whether the patient pays attention to them or not, which accounts for their apparent inconsistency. Naturally these two types of reaction, affective and hysterical, frequently coexist.

2. *The discovery of psychological factors precipitating or causing organic disease.*—That emotional causes can play a part in precipitating chorea, Graves' disease, and other conditions has long received semi-official recognition. The discovery of similar factors in the production of essential hypertension, angina pectoris, and peptic ulceration has gradually led to the

recognition of the importance of psychological as well as of somatic features in the production of many organic states.

3. *Somatic disease in relation to psychological type.*—Some investigators have gone beyond the analysis of psychological causation and the variably important contribution of psychological factors in the origin of somatic symptoms of somatic disease, to the study of personality types in various kinds of physical illness. It should be borne in mind, however, that the psychological traits that may be discerned may not be so much a cause as an indication of the constitutional set-up or predisposition that is manifest in the psychological as well as in the somatic aspect of the total personality.

4. *Psychological reactions to somatic disease or defect.*—Every somatic illness has a subjective aspect in the patient's experience of it. In certain diseases this may be complicated by mental changes due to the disease itself, as in the toxic confusional psychoses. The mental state of tuberculous patients is further complicated by the psychological effects of environmental factors such as hospitalisation and loss of earning capacity. Again, the reactions to a mutilation or injury are conditioned by the type of damage and the age, personality, and sex of the sufferer, as well as his temperament, ambitions, and intelligence.

Obsessional States

Obsessions have been defined as "contents of consciousness which, when they occur, are accompanied by the experience of subjective compulsion, which cannot be got rid of, though on quiet reflection they are recognised as senseless" (K. Schneider).

Minor obsessional symptoms, such as having to count objects, are not unknown among normal individuals. All children tend to ritualise, and nearly all of us have our scruples, and indulge in a special order when we dress or undress.

Obsessions are generally divided into obsessional ideas, impulses, and phobias, and, as has been mentioned, the latter bear a close relation to anxiety and anxiety states. The object of the phobia varies and some types have been given special names, such as claustrophobia, agarophobia, or even erythrophobia, or fear of blushing. Fears of bacteria, or of swallowing harmful substances, or of being soiled, or of touching knives, are other typical examples.

Obsessional impulses show the same variety. Some patients feel forced to touch everything, or to count or to arrange things in a special order. Impulses to commit suicide or homicide are generally mastered unless the obsessional state is complicated by the features of some other syndrome, such as depression. Obsessional patients, in contrast to schizophrenics, struggle against their impulses. Many patients elaborate defence mechanisms against their obsessional impulses, and substitute more harmless actions for those that cause them fear. There is a tendency for these ceremonials to become more and more complicated, which makes the behaviour of many patients with obsessions appear very odd. Similar ceremonials and defence mechanisms develop out of phobias, and patients with a fear of dirt or disease may feel impelled to wash themselves whenever they touch anything; others wear gloves or adopt more complicated devices. Compulsive utterances may also occur, sometimes consisting of meaningless words or phrases, but very

often having a manifest or very slightly disguised content of an obscene kind. The impulse to swear, or to blaspheme, or to be obscene, may be aroused by religious pictures or crucifixes. The obsessional ideas and thoughts may be verbal or musical, or may take the form of visual imagery or pictures. The repetition of meaningless phrases or questions such as : " Why is that so ? " " Why is God ? " " Why is the world ? " " Why is not nothing ? " may become a torture. Others develop doubts and scruples about what they have done, or should do, and must return constantly to see whether the door is shut or the gas turned off ; but the doubt still remains. They have to repeat calculations and make careful notes to see that all is done in proper order. One patient felt impelled to write out the next day's programme in shorthand the night before, taking some hours over this task.

Ætiology.—The pre-morbid personality of obsessional patients frequently shows minor obsessional traits. But these and similar traits not only occur in those who never become mentally ill but also occur in patients who develop mental illnesses that are not of an obsessional type. This makes the ætiological significance of such factors rather limited. Heredity plays an important part, and one-third of the parents of obsessional patients and one-fifth of their siblings have pronounced obsessional traits. The obsessional symptoms can often be traced back to wishes and experiences that have given rise to painful emotions, and have therefore been repressed. The repression is kept up by the strict self-discipline that is so characteristic of the obsessional person. These psychological considerations do not explain why the results of repression take an obsessional form, and it is usually assumed that they develop on a constitutional background. But obsessional symptoms may occur in organic brain disease in patients who have shown no sign of constitutional predisposition. The close connection between obsessions and paroxysmal neurological symptoms, such as the oculogyric crises of post-encephalitic Parkinsonism, makes it probable that in these cases there is a close connection between the psychological and physiological events.

Prognosis.—The prognosis for an obsessional illness depends on the setting in which it occurs. When obsessional symptoms are present or when obsessional characteristics become more acute within the setting of a depressive state, the prognosis is good. Certain patients have one or more recurrent obsessional upsets without much evidence of depression. But when the onset is gradual, the progress slow, and when the symptoms tend to become more and more elaborate, the prognosis is poor. Severe obsessional symptoms may preclude the patient from all work and social activity, and induce a life of seclusion scarcely to be distinguished from that of a schizophrenic illness. Severe obsessional symptoms in youthful individuals not infrequently pass into a definitely schizophrenic illness later.

In a follow-up study, made many years after discharge upon an unselected group of obsessional patients, it was found that one-half were well, one-third stationary or worse, and the remainder ran a fluctuating course (Aubrey J. Lewis).

The **differential diagnosis** in chronic obsessional neuroses from schizophrenia may be difficult, for the emotional response of such patients is often poor and queer. It is essential for the correct diagnosis that the criteria for an obsession should be fulfilled, and that the compulsion should be fought against and not projected as something coming from the outer world.

The **treatment** will depend on the setting. Patients with depressive

components must be treated like depressive states. A carefully planned regime assists some patients to overcome their difficulties, and a change of surroundings—such as admission to hospital—often leads to some improvement. Prolonged psychotherapy can hardly claim more therapeutic success than that achieved by the more reserved activity of an out-patient department.

As has been mentioned previously, prefrontal leucotomy should be considered in severe long-standing obsessional states. Life is often intolerable for such patients, and excellent results can be obtained.

THE LEGAL ASPECTS OF MENTAL ILLNESS

Admission of Patients to Mental Hospitals

A patient may be admitted to a mental hospital, or other premises approved by the Board of Control, (1) as a voluntary patient, (2) as a temporary patient, and (3) as a certified patient.

1. **Admission as a Voluntary Patient.**—The patient has to sign a form of application expressing the desire to be treated as a voluntary patient, with the understanding that, should he desire to leave, he may do so on giving seventy-two hours' written notice to that effect. No other formalities are required. If the patient is under the age of sixteen, a parent or guardian has to sign the form of application which, in this case, must be accompanied by a medical recommendation.

2. **Admission as a Temporary Patient.**—This method also avoids certification, but is only applicable to a patient with a good prognosis who is likely to benefit from the treatment, and who is "incapable of expressing himself as willing or unwilling to receive such treatment." Unfortunately, only a small percentage of patients fulfil these criteria.

An application has to be made by the husband, or wife, or near relation, and two medical recommendations are required, one to be signed by a medical practitioner approved by the Board of Control for the purpose, the other, if possible, by the patient's usual medical attendant. The practitioners may examine the patient separately, but within seven days of each other, or together; and the medical recommendations are valid for fourteen days after the date of the later of the two examinations.

The primary period of detention must not exceed six months, but if signs of impending recovery are evident, the detention may be extended, by three-monthly periods, up to a year from the date of admission.

3. **Admission as a Certified Patient.**—There are four methods of certification in England, and it is convenient to consider them (A) as applicable to private patients and (B) as applicable to rate-aided patients, *i.e.*, patients who cannot afford to go to private institutions but must go to rate-aided hospitals.

A. *For Private Patients.*—(1) *By Reception Order on Petition.*—Five separate documents are required:—

(*a*) A petition addressed by the nearest relation to the appropriate judicial authority, usually a Justice of the Peace, especially authorised for the purpose.

(*b*) A Statement of Particulars, *i.e.*, age, profession, etc., of the patient.

(*c*) and (*d*) Two Medical Certificates, one of which should, if possible, be signed by the patient's usual medical attendant. The medical examinations must be carried out separately, and must be made within seven days of the presentation of the petition.

(*e*) The Reception Order, which must be signed by the judicial authority to whom the petition is presented.

(2) *By Urgency Order*.—Three documents are necessary, but are all available on one form :—

(*a*) The Urgency Order addressed to the Medical Superintendent, or person in charge of the institution, to which the patient is sent. This must be signed by the nearest available relative.

(*b*) A Statement of Particulars, as in (1).

(*c*) One Medical Certificate.

The urgency order remains in force for seven days, and during this period the patient may be discharged, or alternatively, he may be certified according to the procedure laid down in (1).

This method has great value when the problem of dealing with the patient is an urgent one, for it avoids the delays that nearly always attend full certification.

(3) *By Summary Reception Order*, and (4) *By Inquisition*.—The former is a method available for non-rate-aided patients in special circumstances, *i.e.*, when found wandering at large, or neglected, or cruelly treated by their relatives. The latter method is hardly ever used, except when large and complicated financial issues arise. Details should be sought in textbooks of medical jurisprudence.

B. *For rate-aided patients* (not private) the method is by *Summary Reception Order*. The necessary forms for admission comprise an order of a Justice of the Peace, a Statement of Particulars, and one Medical Certificate.

In practice, when a patient cannot afford an institution for private patients, the medical attendant should advise the relatives to notify the Relieving Officer of the district (his address can, if necessary, be obtained from the police). It is well to give the relatives a note to the effect that the patient is a fit case for removal to the observation ward, with a brief outline of the reasons that have led to this conclusion. The Relieving Officer will then make the necessary arrangements. Such a note is not a certificate.

The reasons for certifying a patient have been summarised as follows :—

1. To protect the public from injury.
2. To protect the patient from self-injury.
3. To give treatment with a view to cure or amelioration which cannot otherwise be given.
4. To protect the patient from injury resulting from want of care.

All the documents connected with certification must be filled up with meticulous care, and reasons have to be given in the medical certificate not only for the patient being of unsound mind but also for his being " a proper person to be detained under care and treatment." Certificates should only give plain statements of fact and should be couched in non-technical language. The diagnosis is not required and should not be given. Facts observed by the examiner must be distinguished very clearly from the facts communicated

by others. The ideal certificate is one that would convince the most stupid and bigoted member of a jury that the patient was insane.

" Persons signing medical certificates will not be liable to any civil or criminal proceeding if they act in good faith and with reasonable care."

Criminal Responsibility

A person who is found to be insane at the time of trial shall not be tried (Criminal Lunatics Act, 1880). When during the trial of an accused person he is found to have been insane at the time of the commission of the act, the jury shall, if satisfied that he committed the offence, return a verdict of " Guilty but insane." In either case the person may be detained in custody during His Majesty's pleasure.

In dealing with insanity the Courts follow the rules laid down by the judges in connection with the case of McNaughton, a paranoid patient who had been tried for the wilful murder of Sir Robert Peel's private secretary. The important points in these rules are :—

1. " In order to establish a defence on the ground of insanity, it must be clearly proved that at the time of committing the act the party accused was labouring under such defect of reason from disease of the mind as not to know the nature and quality of the act he was doing, or if he did know it, that he did not know he was doing what was wrong."
2. " If the accused labours under ' partial delusions ' only, and is in all other respects sane, he should be considered in the same situation as to responsibility as if the facts with respect to which the delusion exists were real."

Modern psychiatry would object to the basic conceptions of both these rules. Thus the idea of partial insanity contradicts the present view that mental disease is a disorder of the total personality, and it is now believed that instinctual and emotional factors are much more important in controlling a person's actions than are intellectual processes or rational considerations. However, these rules are still applied in court.

Civil Law

The question of insanity may arise in all provinces of Civil Law, but only three points will be mentioned here :—

1. **Management of Property.**—If a person is apparently unable to manage his property by reason of mental disorder, a guardian may be appointed for him, and the Master in Lunacy is empowered to exercise jurisdiction over the estate of mental patients and, if necessary, to appoint a receiver.

It is possible under Section 116 of the Lunacy Act, 1890, for a doctor, who ought to be the patient's usual medical attendant, to write a certificate to the effect that the patient is incapable of managing his affairs " by reason of mental infirmity arising from disease or age," and this can be made to apply to those who are not certified. This provision is extremely useful for senile patients and for certain other conditions.

" If the patient is lawfully detained the Master is in a position, if he thinks it desirable, to make an order without requiring any medical evidence."

2. **Testamentary Capacity.**—This is not an uncommon question in examinations. The medical man should satisfy himself on the following essential points: Does the patient (1) understand the nature of a Will; (2) the effect of a Will; (3) appear to have a reasonable knowledge of his estate and has he any delusions thereon; (4) has he the capacity to appreciate which dependants, relatives, or friends might reasonably be entitled to his bounty; (5) has he any delusions which would *per se* cause him to omit any person or persons as beneficiaries, who otherwise might reasonably have been included; (6) has he any delusion which would cause him to make a gift which he might not have made in the absence of such delusion; (7) does he appear to understand the importance attached to his act; (8) if the medical practitioner sees the draft of the will, do the bequests appear to him to be reasonable.

A patient who is certified may possess testamentary capacity and one who is not certified may not.

Divorce.—Insanity can be a reason for divorce and for nullification of a marriage. A petition for *divorce* may be presented on the ground that the respondent is "incurably of unsound mind and has been continuously under care and treatment for a period of at least five years immediately preceding the presentation of the petition" (Matrimonial Causes Act, 1937). "Under care and treatment" means either certified or a voluntary patient, provided the voluntary treatment follows directly on a period of detention under a certificate.

Nullification of a marriage may take place if either party was at the time of the marriage of unsound mind, or a mental defective, or subject to recurrent fits of insanity or epilepsy. The condition of such a decree is that the petitioner was at the time of the marriage ignorant of the facts alleged. The petition has to be filed within a year from the date of marriage. With regard to nullification no details about the type or degree of insanity have as yet been laid down; at any rate, certifiable insanity is not the only necessary condition.

All the necessary forms in connection with the legal aspects of mental illness may be obtained from Messrs Shaw & Sons Ltd., Fetter Lane, E.C.4, or from the institution to which the patient is to be removed.

The Board of Control, the central authority in England, expresses willingness to provide help and information in tackling questions referring to certification, but is not able to pronounce whether a patient should be certified, though it may question the legitimacy of certification subsequently.

DESMOND CURRAN.
ERIC GUTTMANN.

COMMON DISEASES OF THE SKIN

THE ERYTHEMAS

ERYTHEMA or redness of the skin due to vascular dilatation is the commonest cutaneous reaction to all kinds of stimuli whether external or internal.

Erythema may be diffuse or disposed in circumscribed spots or patches, and it may be generalised or of limited distribution. Active erythema is generally bright red in colour and accompanied by more or less tenderness, burning, and itching ; the surface temperature is usually raised. The colour of passive erythema is dark red, or even violet, and the temperature of the skin is lowered. Blanching of erythema is produced by pressure. Simple erythema may be complicated by serous exudation, cellular infiltration, and hæmorrhage in the skin with the formation of elevated lesions of various dimensions and colours, sometimes surmounted by bullæ or vesicles.

Classification.—Excluding all due to external causes, the important erythemas may be classified as follows :—

A. *Erythemas of Limited Duration.*—1. The eruptions of rubella, typhoid fever, typhus, scarlet fever, and the roseola of syphilis ; prevariolar erythema, and the erythemas which may accompany puerperal fever and other septicæmias, cholera, and cerebrospinal meningitis. All these have been described elsewhere.

2. Erythematous rashes may follow the administration of an enema or of drugs, especially opium, mercury, quinine, copaiba, phenolphthalein, the iodides and bromides, antipyrine, salicylates, digitalis, belladonna, the sulphonamide drugs, and the barbiturates. A detailed description of these is beyond the scope of this chapter.

3. Erythema scarlatinoides.

4. Recurrent scarlatiniform erythema.

5. Erythema nodosum (*vide* p. 62).

6. Erythema multiforme.

B. *Persistent Erythemas.*—1. Annular centrifugal erythema. 2. Lupus erythematosus. 3. Erythema pernio. 4. Acrocyanosis. 5. Rosacea (*vide* p. 800).

Erythema Scarlatinoides.—The onset is acute and may be accompanied by slight to moderate fever, which may last a few days. The eruption, bright red in colour, resembles that of scarlet fever. The distribution is widespread, but part of the surface may be spared ; the face may or may not be involved. Exfoliation commences on the third or fourth day, earlier than in scarlet fever and often before the disappearance of the erythema. Redness of the mucous membranes of the nose and pharynx and exfoliation of the tongue usually accompany the eruption. The skin returns to its normal condition in about three to four weeks.

The diagnosis from scarlet fever may be difficult in the early stage, but the whole process is of shorter duration.

The eruption may follow the administration of an enema or of certain

drugs, notably opium, quinine, and mercury. It may occur in acute rheumatism, tonsillitis, septicæmia, pyæmia, and food poisoning. In many cases, however, no definite cause can be established. A recurrent and usually more severe form of the condition is known as recurrent scarlatiniform erythema.

Erythema Multiforme.—A variety of eruptions consisting of raised erythematous lesions of figured outline and of various dimensions are included in this group.

Symptoms.—There are four main types of lesion, erythemato-papular, erythemato-vesicular, bullous, and nodular. They are accompanied by pruritus and burning, and occur generally in numbers on the following sites of predilection ; the dorsal aspects of the fingers and hands, the forearms and elbows, the face—especially the forehead—the feet, ankles, legs, and knees. Other parts of the body may also be attacked. Lesions also occur frequently on the buccal mucous membrane, especially in recurrent cases, and are occasionally limited to that situation.

The disease, which runs a course of two to four weeks, may begin with slight initial fever, or exceptionally there may be moderate fever lasting a week or longer. Constitutional disturbance is usually mild in degree or absent, but there may be pains in the limbs and gastro-intestinal disturbance, sometimes with vomiting, diarrhœa, and passage of blood in the stools. Erythema multiforme occasionally occurs in acute rheumatism.

Recurrences are common.

Erythemato-papular Type.—The lesions are raised lenticular papules or patches, exhibiting a central zone which may be violet in colour, or pale from œdema, or hæmorrhagic, surrounded by a peripheral red zone ; delicate transitions in tint from one zone to another are often seen.

Erythemato-vesicular Type.—The peripheral zone is surmounted by a row of vesicles which may become confluent to form a continuous ring.

Bullous Type.—The centre of the lesion is surmounted by a bulla ; the peripheral zone may be vesicular.

Nodular Type.—The lesions resemble erythema nodosum, but are smaller and usually brighter red in colour. One interesting variety of this type persists if untreated for many months, accompanied by fever and joint pains, but without severe constitutional symptoms. That it is due to meningococcal septicæmia has been proved by blood culture on many occasions. It is cured rapidly by the administration of sulphonamides.

The lesions on the mucous membrane begin as erythematous patches or bullæ, which quickly become eroded to form rather painful shallow ulcers, often covered by a slough.

Erythema multiforme is a cutaneous reaction of multiple ætiology. It is an expression of individual sensitivity to toxins derived from various sources. A lesion in the skin itself, such as a whitlow, a burn, or pustular ringworm infection are occasional focal causes. The recurrent cases have usually no discoverable cause. It is possible that there are really two groups : (i) those in which the eruption is the expression of allergic sensitivity to a demonstrable infection ; the mucous membranes are rarely affected and recurrences are uncommon ; (ii) cases which occur in the complete absence of any other disturbance, and which, like herpes simplex, recur at long or short intervals. The mucous membranes are often attacked ; for these there may be a specific, though at present unknown, cause.

Treatment.—In view of the fact that erythema multiforme may be an

expression of a serious condition such as acute rheumatism, it is advisable to regard all initial attacks as potentially serious, and to advise confinement to bed. When past attacks have been unaccompanied by constitutional disturbance, this measure may be unnecessary ; but a general examination should always be made, particular note being taken of any elevation of pulse and temperature.

The treatment of recurrent cases is disappointing, but in general it should be directed towards the eradication of possible foci of infection, particular attention being paid to the teeth, tonsils, and sinuses.

Fortunately, the condition does not tend to recur throughout life, but disappears in the course of years.

The local treatment is of little importance, and consists of the alleviation of burning and pruritus by the application of soothing liniments or creams ; calamine lotion or liniment serve this purpose.

Stevens-Johnson Syndrome.—An erythemato-bullous eruption of the erythema multiforme type but presenting special and striking features is met with occasionally. The onset is acute with fever ; blisters and erosions occur first on the mucous membrane of the mouth and sometimes on the conjunctivæ ; this is followed within a few days by a widespread eruption consisting of erythematous spots and patches with a tendency to form blisters, particularly about the mouth and on the genitals. Fever persists for ten to fourteen days, and during this period the patient may be ill ; a few cases have died. Rapid recovery follows the fall in temperature. The ophthalmia may be severe and has occasionally led to blindness. The cause of this condition, named by Stevens and Johnson eruptive fever with stomatitis and ophthalmia, is unknown. It has occurred at intervals with some frequency. Its course is uninfluenced by treatment with either sulphonamides or penicillin.

Annular Centrifugal Erythema.—This not uncommon type of erythema consists of raised red patches, which enlarge peripherally by a raised cord-like border and clear in the centre to form annular, or by confluence with other lesions polycyclic, figures. They extend gradually, and in the course of weeks may attain a diameter of several inches. The centre is usually faintly pigmented.

The eruption occurs on any part and there may be several lesions or only one ; after several weeks or months they ultimately disappear. Recurrences are sometimes seen, often at the sites of previous lesions.

Lupus Erythematosus.—*Symptoms.*—The lesions of this important disease consist of slightly infiltrated patches of persistent erythema covered with adherent scales. The patches are of oval, round, polycyclic, or irregular outline, and have a tendency to clear up in the centre with the production of scarring. The scales may be lamellated or fine, or may be present only in the mouths of the hair follicles as horny plugs.

The lamellated scales often show on their under-surfaces horny prolongations which project into the follicles. Lesions which have undergone partial healing with atrophy often have a depressed centre and a raised border.

Telangiectases are generally seen both in the atrophied portion and on the actively spreading border. The lesions are the seat of mild burning sensation and occasionally of itching, and may be tender to touch. There are four types, three of them of limited distribution and usually symmetrical, the fourth disseminated ; they are : the fixed type ; a wandering symmetrical

type, Lupus erythematosus migrans; (3) Hutchinson's chilblain lupus: disseminated Lupus erythematosus.

The Fixed Type.—The disease occupies especially the bridge of the nose and the malar regions, the temples, scalp, ears, and the backs of the hands and fingers, especially the terminal phalanges. One or several patches may be present. The lesions are infiltrated, scaly, and extremely persistent, healing with marked atrophy and adhesion of the scar to such underlying tissues as the cartilages of the nose and ear. Lesions consisting of a middle red zone or band bordered with a white zone resembling leucoplakia are met with on the buccal mucous membrane in about a quarter of the cases. *Lupus erythematosus migrans* begins with bright red congestive patches, most often on the cheeks; they extend with some rapidity forming eventually by confluence with others more or less extensive areas. They tend also to clear up in the centre, usually with just detectable atrophy, while the peripheral portion remains red, turgid, and usually covered with fine scales. These cases, more unstable than the fixed type of the disease, are also more widespread as a rule. It is common to find lesions on the neck and the chest, as well as on the hands and forearms. They link fixed Lupus erythematosus with the disseminated cases, and they are sometimes classified as subacute.

Hutchinson's Chilblain Lupus.—The condition described by Jonathan Hutchinson as chilblain lupus is Lupus erythematosus, confined to the hands. The lesions resemble chilblains to begin with, but become depressed in their centres and scaly, and ultimately heal with atrophy. They occur chiefly on both palmar and dorsal aspects of the fingers, but often on other parts of the hands as well. Atrophy with telangiectases can almost always be seen on the dorsal aspect of the terminal phalanges. The condition often clears up in summer, though scars remain.

Disseminated Lupus Erythematosus.—This may occur either as an extension of one of the preceding types, or it may be acute and disseminated from the beginning. It is relatively rare.

The onset is acute with fever and often with severe constitutional disturbance. The eruption is in the form of widespread patches and sheets, red or violaceous in colour, and finely scaly; scattered bullous lesions may rarely be present. The distribution is more or less universal. These cases may be fatal in the course of several months, or they may regress. Relapse after remission, even of long duration, is, however, the rule rather than the exception. In fatal cases death is due to broncho-pneumonia, pericarditis, pleurisy, septic arthritis, and other types of septic infection, occasionally to generalised tuberculosis. The rare condition known as Libman-Sachs syndrome is acute lupus erythematosus accompanied by endocarditis of a special type. Peculiar wart-like vegetations are found on the cardiac valves on either side of the heart.

Ætiology.—Lupus erythematosus is very rare in children and somewhat less rare in old age; it occurs chiefly between twenty and fifty years of age. The sites of predilection are those in which the peripheral circulation is most stagnant—the nose, cheeks, ears, and fingers. The influence of cold is demonstrably important, also that of sunlight. We do not know how these physical stimuli provoke the changes characteristic of Lupus erythematosus, but evidently they alone cannot be responsible.

It has long been believed to be related to tuberculosis; the existence, however, of tuberculosis elsewhere can rarely be demonstrated, and

histologically the disease bears not the least resemblance to tuberculosis. However, the coexistence of the two conditions is occasionally met with in the chronic types, and as already stated, a few of the acute cases terminate with generalised tuberculosis. It seems therefore probable that in some at least tuberculosis plays a part.

It is possible also that other infections may be concerned in the process, and it has been suggested that because many fatal disseminated cases terminate with some streptococcal complication, some of the chronic cases may be due to latent or focal streptococcal infection.

Treatment.—Lupus erythematosus is extremely chronic and intractable ; while there is a tendency towards more or less spontaneous resolution, particularly of the superficial variety of the disease, attempts to influence it by treatment have in the main proved disappointing. Practical measures consisted in the past of local applications, such as carbon dioxide snow or a mixture of phenol and lactic acid. In more recent years a little progress in the treatment of the disease has been achieved by the use of gold compounds, bismuth, and sulphonamides. Gold preparations are of occasional value in the fixed type, but they are not safe in the more unstable types, whether localised or disseminated. They are administered by weekly injection, a total of about 1 gm. being given in ten to twelve weekly doses. After an interval of two months or longer a further course may be necessary. Subacute cases may be favourably influenced by sulphanilamide, in the dosage of 0·5 gm. two to three times daily. Penicillin has proved ineffective.

Erysipeloid of Rosenbach.—This is a circumscribed erythema of infective origin. It occurs most often on the fingers and hands and bears a superficial resemblance to erysipelas, but as met with in this country there is little or no fever or constitutional disturbance, and only moderate tenderness. A dusky, almost cyanotic hue, is characteristic. Erysipeloid occurs in butchers and others, including housewives whose work involves handling meat. It became far more common in England during the war than formerly. The causal organism is the *Bacillus erysipelatus suis* or *erysipelothrix rhusipathiæ*, and is carried as a saprophyte on a variety of animals and fish ; the infection gains entrance through any small breach on the skin, and often follows a prick by a bone. Erysipeloid usually responds rapidly to penicillin given parenterally ; untreated it clears up spontaneously in from three to seven weeks. A mild, temporary arthritis of one or more joints in the area of the erythema is an occasional complication.

Erythema Pernio (Chilblain).—Chilblains are erythematous swellings which occur in cold weather in individuals who suffer from circulatory hypostasis. Children and adolescents are chiefly attacked. The lesions appear first as erythematous patches, but owing to serous exudation and cellular infiltration quickly become transformed into tumefacient swellings. The dorsal aspects of the fingers and toes, the ulnar margins of the hands, the lateral margin of the feet, the heels, the ears, and nose are chiefly affected. They are accompanied by tenderness, burning and itching, and are sometimes the seat of superficial vesicles or bullæ. The surface is frequently broken by friction, with the production of painful superficial ulcers. In the cold sunny weather of early spring a variety of perniosis, in which the lesions resemble those of erythema multiforme, is occasionally seen in children ; the fingers and ears are attacked.

Treatment.—The development of chilblains may be prevented to some

extent by wearing thick boots, warm stockings and gloves, and especially by active exercise. Calcium by the mouth is a popular remedy, but there is no demonstrable disturbance of calcium metabolism and the treatment is probably of no material value. Vitamin D in large doses is of no value; nicotinic acid by mouth is said to afford symptomatic relief in some cases, and the same claim has been made for vitamin K in doses of 10 to 20 mg. twice daily. Locally stimulating applications may be used. (For examples, *vide* Therapeutic Section).

Acrocyanosis.—As the name implies, this condition consists of a cyanotic congestive erythema of the extremities. The hands, the lower third of the legs, and the feet are especially affected. In severe cases the hands are cold, blue, and moist. On digital pressure the erythema may be made to blanch for as long as half a minute, demonstrating the extreme degree of circulatory hypostasis. The condition is most often seen in adolescent and young adult girls, who are nearly always somewhat obese and exhibit on their lower extremities papular follicular lesions resembling those of keratosis pilaris, which, owing to congestive vascular changes, become reddened and especially prominent in cold weather; this change is often spoken of as follicular perniosis.

Diffuse blue swellings often appear on the lower thirds of the legs in winter, particularly on the outer aspect. They may be somewhat painful, and occasionally become (superficially) ulcerated or the site of bullæ. They are not infrequently mistaken for hypodermic tuberculides (Bazin's erythema induratum).

The condition disappears partly or completely in summer, but recurs each winter for several years; eventually the cyanotic erythema and swellings diminish to be replaced by a podgy thickening of the extremities which is often observed in middle-aged women.

The swellings on the legs may be made to disappear by rest in bed, apart from which, treatment consists in wearing warm stockings and boots and the use of stimulating external applications. Calcium therapy has proved of no value. Relief in severe cases has followed lumbar sympathectomy.

Rosacea and Acne Rosacea.—This condition, which consists essentially of congestive erythema over the forehead, nose, cheeks, and chin, with occasional extension to the neck and ears, is primarily dependent upon changes in the vessels of the skin. These consist of a persistent dilatation of the capillaries and venules which often leads eventually to the formation of telangiectases. Some degree of constitutional vaso-motor instability is commonly present. Rosacea may occur independently of seborrhœa, but when this is present the vascular alterations are frequently complicated by acneiform pustules, and it is for these secondary lesions that patients often seek advice. Digestive troubles are sometimes present and may accentuate the vascular changes in the skin; chronic gastritis with flatulence and the sensation of fullness after meals are fairly common, and in such cases a meal, a hot drink, or alcohol will provoke reflex flushing of the rosaceous areas. The fractional test meal has shown in a small proportion of cases an absent or low free hydrochloric acid content. Rosacea is, however, not uncommon in subjects in whom digestive trouble is entirely lacking. Exposure to hard weather conditions may be the sole apparent cause. No doubt alcohol is a factor in certain rosaceas, but its importance has been exaggerated.

Symptoms.—In the early stage rosacea consists of attacks of congestion.

By degrees this becomes permanent and dilated venules develop, particularly on the cheeks and nose. In seborrhœic subjects acneiform pustulation and hypertrophy of the sebaceous glands take place, and in extreme degrees may lead to severe disfigurement. The nose in particular may be enormously hypertrophied (*rhinophyma*). A small percentage of cases are complicated by corneal ulceration ; this is preceded by extension of the rosaceous congestion of the cheeks to the conjunctiva lining the lower eyelids. Acne keratitis, as it is called, is sometimes found in purely vascular rosaceas, that is, without seborrhœa or acne.

Treatment.—This must be directed primarily to the underlying cause. Septic teeth must be removed and stimulants prohibited. Meals should be simple in quality and small in quantity. In those cases which depend upon chronic gastritis, dilute hydrochloric acid taken with or immediately after meals is often very valuable. Pustular cases often respond satisfactorily to ointments and pastes containing sulphur. The dilated venules and capillaries may be destroyed by ignipuncture or electro-coagulation. Carbon dioxide snow evenly applied for five seconds over the reddened areas will sometimes diminish the persistent erythema. Rhinophyma is best treated by plastic operation.

PYOGENIC INFECTIONS OF THE SKIN

The Normal Bacteriology of the Skin.—Two micro-organisms have a predilection for the sebaceous follicles : the staphylococcus and the acne bacillus. The latter is found in adolescents and adults in the sebaceous and horny material which can be expressed from the follicles in seborrhœic subjects. Staphylococci are found in single elements in a large proportion of all follicles, while the sweat ducts are generally sterile. In addition to these bacteria, yeast-like organisms are found normally in the skin, especially the pityrosporon, which occurs in the scales of pityriasis capitis, and of seborrhœic dermatitis. Streptococci are not found on healthy skin, though they readily become implanted on damaged skin.

Staphylococcal Infections

Isolated staphylococci in the mouths of the follicles are harmless ; when, however, conditions arise which allow them to multiply, they give rise to a reaction in the form of a follicular pustule. This is the primary lesion of the following staphylococcal eruptions : simple staphylococcal folliculitis or Bockhardt's impetigo, furunculosis, carbuncle, hidradenitis, sycosis.

Bockhardt's Impetigo.—The elemental lesion consists of an intra-epidermal pustule, almost invariably situated at the mouth of a hair follicle. Its mode of formation is as follows : growth of the organism determines a flow of serum and leucocytes to the colony of microbes situated in the superficial layers of the epidermis. The leucocytes obtain access to the point of multiplication without obvious damage to the deeper layers of the epidermis, but dislocate the more superficial layers and form a little biconvex intra-epidermal pustule. The reaction results ordinarily in the death of the organism, the pustule slowly dries up into a crust, and is finally cast off the surface by regeneration of the epithelium beneath the crust.

Bockhardt's impetigo occurs commonly on the scalp in children, generally following an attack of impetigo contagiosa, or it may complicate other conditions such as eczema of the scalp or pediculosis. It is often accompanied by painful suboccipital adenitis. The eruption consists of closely aggregated yellow pustules, small or large, each centred by an emerging hair. It occurs also on other parts.

Furunculosis.—The growth of staphylococci is not necessarily confined to the most superficial part of the follicle, but may penetrate to varying depths. When multiplication takes place in the deeper portion of the follicle, one of two reactions may take place: the formation of a perifollicular abscess (furuncular abscess) or sudden massive necrosis of the tissues surrounding the follicle (a furuncle). In either case the deeper infection is almost always preceded by a small superficial pustule which may have disappeared spontaneously before the more important lesion has attained its full development. In the case of an ordinary boil, the staphylococcal colony remains confined to the centre of the process, and the death of surrounding tissue is determined by toxins acting at a distance. By degrees the necrosed mass is either separated from the normal tissue by the advent of leucocytes and detached as a core or as a slough, or it may be converted into an abscess or sometimes absorbed without breaking down. Of the constitutional factors that predispose to furunculosis very little is known. Many intractable cases appear otherwise to be in good health. Diabetes is, however, a well-known predisposing cause. Occasionally furunculosis is accompanied by a glycosuria which disappears with the cure of the infection. In the majority of cases there is no demonstrable disturbance of sugar metabolism.

Furunculosis frequently relapses over long periods, especially in certain places, notably the nape of the neck and the large folds. Seborrhœa and hyperhidrosis are predisposing factors.

Carbuncle.—The ætiology is similar to that of a boil, but the lesions are more extensive. The necrosis of the perifollicular tissue may spread in the subcutaneous tissue to involve several follicles, or a carbuncle may be caused by the simultaneous infection of a number of follicles, the perifollicular necrosis forming a confluent mass in the skin and subcutaneous tissue. Carbuncles are detached by peripheral suppuration and generally end by separating as a slough.

Hidradenitis.—The lesions are intradermal or subcutaneous abscesses found practically only in the axillæ and occasionally in the anal and genital area. They may complicate seborrhœic dermatitis of the axillæ and hyperhidrosis, and are formed about the sweat glands. They begin as one or more painful dermal or subcutaneous indurations, which may be absorbed or may become soft and finally discharge creamy pus through a thin red epidermis; they are never detached as a core as in furunculosis. They are very prone to recur, especially in hot weather.

An attack of furunculosis appears to lower what might be called natural resistance to staphylococcal infection, and attempts to raise it by artificial means have not proved very successful. Treatment by vaccines has to some extent been replaced by graduated injection of staphylococcal toxoid, or a mixture of toxoid and vaccine (vaccoid), by means of which it is possible to raise to a remarkable degree the capacity of the blood to inhibit the lysis of rabbit's blood cells by staphylococcal toxin.

Of other general remedies sulphathiazole and sulphadiazine have been

largely superseded by intramuscular penicillin. The dosage usually employed is 20,000 to 30,000 units at three hourly intervals, or 150,000 units twice a day.

Local Treatment.—In the stage of the early circumfollicular pustule boils may sometimes be aborted by opening and applying pure carbolic acid or by the galvano-cautery, using a fine point, but later than this surgical interference is harmful. Hot Alibour water dressings (*vide* p. 841) or mercury perchloride dressings, the application of pure ichthyol, or magnesium sulphate mixed with glycerin to make a paste, are all satisfactory forms of local treatment. Similar treatment is suitable for hidradenitis, though the softened abscesses often require opening. For this condition short-wave diathermy is also a valuable local remedy. Since the advent of penicillin surgical intervention is seldom necessary in the treatment of carbuncles. To prevent recurrences Sabouraud recommends attempting to sterilise the whole skin by adding zinc sulphate to the daily bath in the strength of 1 in 4,000. Mercury and potassium iodide 4 gm. to the bath may also be employed.

Sycosis.—In this condition the lesions are follicular pustules of the same anatomical form, for the most part, as the pustule of Bockhardt's impetigo, though a certain proportion of the follicles are infected more deeply. The infecting organism is always *Staphylococcus aureus*. There are six clinical varieties :—

1. Sycosis of the upper lip, which is often secondary to chronic rhinitis and is generally accompanied by chronic blepharitis and often conjunctivitis.

2. Sycosis of the scalp, found generally in children as a complication of a chronic impetigo or eczema. This type is also generally accompanied by sycosis of the eyebrows and eyelashes.

3. Sycosis of the face or chin, often called barber's rash ; this often follows impetigo of the beard.

4. Sycosis nuchæ is a fourth variety. The nape of the neck is especially liable both to furunculosis and chronic staphylococcal folliculitis. The latter occurs chiefly in obese subjects with thick necks. Friction of the collar appears to determine the site of the infection in some cases, but in others the folliculitis is above the part which is rubbed in this way ; in these intertrigenous friction of the redundant skin may be the determining factor. Occasionally the chronic follicular infection is accompanied by fibrous proliferation, the pustules being converted by this process into small hard nodules, or when confluent into a horizontal irregular fibrous band. When this occurs the condition is spoken of as dermatitis papillaris capilliti (Kaposi). The same fibrotic change may accompany pustular acne of the nape of the neck.

5. Lupoid sycosis. In this type the follicles are deeply infected and ultimately destroyed. Central cicatricial alopecia is accompanied by a very gradual centrifugal spread of the infection. The condition is generally found as a single plaque on one cheek, or as a more or less widespread area in the scalp.

6. Generalised sycosis ; the scalp, eyebrows, eyelashes, beard, axillary, and pubic hair follicles are all affected. These cases are often late sequelæ of chronic eczema of the infective type or sycosis of the scalp in childhood.

Symptoms of Sycosis.—The lesions consist either of more or less closely aggregated follicular pustules, situated on a diffusely red background, or tuberous lesions in the positions already described, or of diffuse red areas, often crusted in parts, in which isolated follicular pustules may not be seen.

They are often associated with fissures at the nasolabial junction and the labial commissures ; they differ from simple folliculitis by behaviour rather than by their appearance in being essentially chronic or constantly recurrent. A certain number of the follicles are deeply infected. Some cases of sycosis end after twenty years or more by cicatricial alopecia of the affected part.

Course and Prognosis.—Sycosis shows little tendency to spontaneous cure, but varies greatly in its response to treatment : the earlier and more localised the case, the greater the probability of complete cure. If the condition has been established for a year or longer, the prognosis is uncertain. Among the more unsatisfactory are the cases which have begun in childhood as an infection of the scalp and eyelashes ; in these the beard is often attacked in adult life. Ciliary sycosis alone, especially if accompanied by chronic nasal catarrh, may also be complicated in adults by intractable sycosis of the upper lip, and sometimes of the beard generally.

The most refractory form of all is that in which all hairy parts are attacked. In many of these the infection in the scalp, or blepharitis, has been present from childhood.

Treatment.—No general treatment can be applied to all cases of sycosis, but any defect in the general state of the patient must receive attention. In early cases with debility from such causes as malnutrition, overwork, or alcoholism, a long holiday in the open air may be of great value. Vaccines have been employed for many years but have not proved reliable. Staphylococcal toxoid has also failed as a remedy for sycosis. Temporary improvement may sometimes follow treatment with sulphathiazole or sulphadiazine but rarely a complete remission ; the effect of penicillin by injection has been equally unimpressive.

The local treatment is of great importance. It is first necessary to stop shaving, keeping the hair cut as short as possible with scissors. Crusts must be removed by starch and boric poultices or antiseptic compresses. Alibour water is a suitable preparation for this purpose diluted with 5 to 10 parts of water.

When the crusts have been removed the improvement is often striking but progresses no further. In early cases it is sometimes possible to complete the cure by the application of one of several preparations, of which one of the most useful is Compound Quinolor Ointment (Squibb). In the event of failure to obtain a remission with the above remedies, sodium sulphacetamide (5 per cent.) or penicillin lotion (1,000 units to 1 c.c.) may be used. These are often a good deal more effective than the older remedies, but they may provoke sensitivity.

In well-established but limited cases it may be necessary to epilate the infected areas by X-ray. In the majority this proceeding is followed by complete relief from symptoms, but in some a close observation of the affected parts reveals bluish or faint red patches which indicate that the infection persists below the surface. The depilated area should receive regular local treatment, and it is here that treatment by spraying thrice daily or painting with penicillin lotion can be most usefully applied. In the case of sycosis of the upper lip, the nose, particularly the vestibule—a frequent source of reinfection—should be treated in the same manner. It is impossible to forecast the result of a single epilation in sycosis ; in some complete and permanent cure follows, but in others regrowth of the hair is followed either immediately or after a short period of freedom by relapse.

Sabouraud recommended after the first epilation the continued removal of the hair, including down, by forceps.

Sycosis of the Eyelashes.—The eyelids are red and thickened ; the lashes are often spontaneously shed, but this does not lead to cure as in sycosis elsewhere. Conjunctivitis is a common complication. *Ciliary Sycosis* frequently complicates impetigenous eczema of the scalp, and is often found in association with sycosis of the upper lip and with chronic rhinitis following measles.

Pemphigus Neonatorum.—This condition, occurring in the first few weeks of life, is not uncommon. The source of infection may be a septic umbilical cord, or the infection may be carried by a midwife from one infant to another. The condition begins as a vesicle which rapidly becomes a large bulla ; this is quickly broken, but the lesion continues to spread peripherally, splitting up the horny layer. The lesions may be comparatively small, but frequently large irregular red areas are found, often quite dry and bounded always by a white collar of detached horny layer. The contents of the vesicles rarely become purulent. Fatal cases have occurred, though the great majority are mild and easily cured.

Pemphigus neonatorum is generally thought to be the counterpart of impetigo contagiosa in adults ; the causal organism is the *Staphylococcus aureus*.

Mixed Infections

While staphylococci have long been recognised as the cause of the foregoing eruptions, it was generally thought until recently that streptococci were responsible for impetigo contagiosa, ecthyma, and fissured impetigo. The primary blister of impetigo contagiosa, except in impetigo neonatorum, has been regarded as particularly characteristic of superficial streptococcal infection of the skin. Recent work, however (J. W. Biggar and G. H. Hodgson, and H. L. Sherwin and Ferguson Girdwood), appears to have upset this view ; both sets of observations showed that in the earliest stage of the infection, that of the primary blister, only coagulase positive staphylococci can be found, while pyogenic streptococci appear later and with increasing frequency the longer the infection has gone on, appearing thus to be secondary invaders. Inoculation experiments with living cultures of staphylococci grown from cases of impetigo contagiosa were also successful, while streptococcal cultures from the same source failed to reproduce the lesions characteristic of impetigo. These observations suggest that streptococci may be responsible for the more persistent types of impetigo or lesions frequently associated with or complicating it, ulcers, fissures, and perhaps the scaly lesions known as impetigo pityrodes.

Impetigo Contagiosa.—The earliest lesion is an intra-epidermal vesicle filled with sero-fibrinous exudate. This quickly coagulates, ruptures, and forms a yellow crust ; at the same time the exudation continues at the circumference of the lesion, splitting up the horny layer. In this way the lesion enlarges and in so doing rapidly becomes covered by a fresh crust.

Sometimes quite large bullæ are formed before the lesion is broken, particularly upon surfaces where the horny layer is thick, such as the palmar surfaces of the hands and fingers.

Impetigo contagiosa is more common in children than in adults ; it is

caused by contagion, when the face, neck, and scalp are most often attacked, or it may complicate other conditions, such as papular urticaria, eczema, and particularly the common parasitic infections, scabies, and pediculosis capitis.

Pityriasic Form (*Pityriasiform Impetigo*).—When impetigo has been cured irregular scaly patches, faintly pink in colour, are often left behind and remain for a variable period on the site of the original lesions. The same scaly lesions may occur spontaneously in children and occasionally in adults, usually in the immediate neighbourhood of the nose or mouth, and in relation to nasal discharge or oral sepsis. Fissures at the labial commissures and at the nasolabial junction are often seen in such cases.

Ecthyma.—This is met with most often in children and may begin as the ordinary type of impetigo, but under the influence of decreased general or local resistance the skin is more deeply attacked and superficial epidermic infection becomes dermic ulceration.

The lesions are round conical ulcers with a tender red margin. They generally become covered by a thick crust, often rupial in appearance, beneath which pus accumulates. They are found usually on the lower limbs, but are auto-inoculable, and as a rule the fresh lesions, wherever formed, are also ulcerative. Occasionally they give rise to lymphangitis.

Fissured Impetigo.—Fissures occur in the course of ordinary impetigo, in the post-auricular sulci, the labial commissures, at the nasolabial junction, the webs of the toes, and in any other natural fold of the skin. They occur in these positions also in relation to other conditions, such as chronic rhinitis, septic tonsils, carious teeth, eczema of the scalp extending to the neck and ears, chronic eczema of the interdigital spaces, and eczematoid ringworm of these spaces. Fissures in the nares and less often on the under surface of the toes are sometimes complicated by a cellulitis of the neighbouring areas, somewhat resembling erysipelas, though with little constitutional disturbance. The attacks last about a week, recurring at intervals until the site of the infection has been cured. Recurrence over a long period may lead to blockage of lymphatics and permanent œdema of the eyelids and adjoining parts of the face and forehead.

General Treatment.—Impetigo contagiosa usually demands no special general treatment. An open-air life, sunlight, and good food are of value in the more chronic types of infection. Ultra-violet light therapy applied to the general surface and locally has also proved of some value. Heliotherapy is the ideal treatment for chronic cases who pigment normally. Sulphathiazole, 1 gm. four times daily for four or five days, or parenteral penicillin, are often rapidly effective, but owing to the risk of provoking sensitivity these remedies ought not to be employed except in the most refractory cases.

Local Measures.— *Impetigo Contagiosa.*—The essential part of treatment is to keep the lesions clean. Various lotions are used for the purpose of removing the crusts; this should be done twice daily and not forcibly. Hydrogen peroxide 3 to 5 vols., Alibour water (*vide* p. 841), or $\frac{1}{2}$ per cent. lysol are generally satisfactory though occasionally irritating. A 5 per cent. solution of sodium sulphacetamide has usually proved very efficient, and if used, no other remedy is required. Other sulphonamide drugs, especially sulphathiazole, incorporated in various types of base have been used, and generally with success. Allergic sensitivity to these is, however, by no means unknown, whether they are applied locally or taken by mouth. They have

provoked an acute light-sensitiveness, a severe bullous eruption, particularly on the exposed parts, or a widespread dermatitis. Penicillin lotion, 500 units to 1 c.c., applied three times daily by spraying or painting is often rapidly effective, but like the sulphonamide drugs it may cause an acute dermatitis. Among other remedies suitable for application after removal of scabs should be mentioned $\frac{1}{2}$ to 1 per cent. solution of silver nitrate, or $\frac{1}{2}$ to 1 per cent. solution of gentian violet in calamine lotion.

Fissures.—A 1 or 2 per cent. solution of silver nitrate in spirit of nitrous ether is a proven remedy. The fissures are painted once a day.

Ecthyma.—The treatment is the same as for impetigo, but it may be desirable to use hot diluted Alibour water or mercury perchloride $\frac{1}{1000}$ in 1 per cent. saline as a fomentation for about an hour twice daily, the lesions being covered in the intervening period with acriflavine in paraffin 1 in 1,000, a weak mercurial ointment or paste. Spraying with penicillin lotion 500 to 1,000 units per cubic centimetre may be used in refractory cases. Rest in bed is sometimes necessary.

Pemphigus Neonatorum.—Potassium permanganate baths (1 in 10,000), followed by gentian violet $\frac{1}{4}$ to 1 per cent. in calamine lotion, is usually a satisfactory treatment.

SEBORRHŒA AND ITS COMPLICATIONS

The term " seborrhœa " means excessive sebaceous secretion. It exists in two forms :—

1. Seborrhœa oleosa, in which the sebum is usually mixed with sweat and gives to the skin an oily, shiny appearance.

2. Cystic seborrhœa, in which the sebum, mixed with epithelial detritus, fills up the upper third of the hair follicle in the form of a greasy plug, which can be expressed from the follicle as a filament.

Seborrhœa, however, is not in itself a disease but a manifestation of a common underlying state of the skin, which has been named " kerosis " by Darier. Darier defines this state as consisting of (i) a dirty-grey discoloration of the skin ; (ii) a patulous condition of the follicular orifices ; (iii) elevation of the follicular collar ; (iv) slight general thickening of the integument. The condition is present chiefly close to the median line, and is found especially on the nose and cheeks, forehead, scalp, nape of the neck, presternal and interscapular regions, and sometimes on the pubes and sacrum. It is usually associated with more or less hyperhidrosis.

Seborrhœa may become manifest in infancy, either in the form of slight oiliness affecting the face chiefly, or very rarely as comedo acne (grouped comedones of infancy).

After a quiescent interval, during which sebaceous activity diminishes, the secretion becomes abundant during puberty. This may result in acne vulgaris, and at a slightly later period in pityriasis capitis and seborrhœic dermatitis. Later again acne rosacea and rhinophyma may be met with in the subjects of kerosis.

Facial kerosis and seborrhœa may occur in marked degree in young subjects after encephalitis lethargica ; in such cases it is generally associated with Parkinsonian rigidity and excessive salivation.

Acne

The primary lesion of acne is the comedo. This consists of a plug composed of sebum mixed with horny and epithelial detritus which fills the upper third of the follicular canal, the mouth of which is blocked by a black horny cap. Some of the lesions, however, exist in the form of retention cysts, large or small. They are found on the forehead, the nose, nasogenial furrows, the cheeks, chin, neck, ears, back, shoulders, and chest, rarely on the sacrum, buttocks, and extensor aspects of the thighs. In addition to sebum and epithelial debris, the seborrhœic plug contains myriads of very small bacilli known as acne bacilli. Comedones frequently become pustular owing presumably to infection of retained sebaceous material. Staphylococcus albus is grown from these pustules, and according to Sabouraud, the acne bacillus may also develop pyogenic activity. There are several clinical varieties of acne.

1. Seborrhœic plugging of the follicles with few actual comedones but with marked kerosis, a condition which renders the face unsightly by reason of the greasiness and coarseness of the skin.

2. Comedo acne, with large numbers of comedones.

3. Comedo acne, with pustules.

4. Cystic acne. There are comedones and pustules, but particularly a large number of cysts, some of considerable size, occupying the cheeks, the neck, shoulders, chest, and back. These patients are often somewhat obese and physically soft.

5. Acne conglobata. This type is somewhat similar to the above in that the lesions are cystic to begin with, becoming eventually soft abscesses which break down and become covered with rupia-like crusts ; by confluence and scarring, labyrinths connected by fistulous tracts and fibrous bridges are formed. The shoulders and trunk are chiefly attacked. This type is met with chiefly in middle life.

6. Acne indurata. This name has been given to a variety of acne, the lesions of which consist of somewhat solid papular and nodular elevations which appear to arise beneath the skin and which slowly approach the surface, become red or blue, and sometimes eventually soften and discharge a cheesy material. The lesions are often almost entirely confined to the chin and may be unaccompanied by comedones. This variety is found almost exclusively in women. It is usually at its worst immediately before and during the period.

7. Oil acne. Contact with various oils and greases may provoke acne, not only on the face but on parts not normally subject to the condition. During the war, the number of these cases increased enormously, particularly among the operators, male or female, of small capstan lathes. They wear protective rubber aprons, but it is not possible to protect the arms and legs, which become the seats of innumerable tiny blackheads and acne pustules ; the hands are spared. Acne, if already present on the face, is aggravated. Oil acne disappears slowly after cessation of contact with oil.

8. Chlorine acne. Halogens provoke, in susceptible subjects, an acneiform eruption in the places normally subject to acne, when taken by the mouth (bromides and iodides) ; and it is supposed that they do this by reason of their excretion, in part through the sebaceous glands. It seems that these glands may also have an affinity for halogens, for an intense

degree of acne occurs frequently in occupations involving external contact with chlorine.

Treatment of Acne.—The common comedo acne of puberty and adolescence has a tendency to disappear spontaneously, though the most severe degrees of it may persist. It is not usually associated with any defect in general health, and the only general treatment of any value consists in maintaining the highest possible degree of physical fitness. Local treatment consists of frequent washing with soap and water, expression of comedones with a comedo expressor, and the application of an exfoliating lotion or paste containing sulphur. As an alternative to exfoliating preparations, ultra-violet light may be used. Small repeated applications of superficial X-ray, which has a selective depressant action on sebaceous cells, are more effective than any other agent, but should only be applied in urgent cases, and with extreme care.

For the other varieties of acne, treatment is less satisfactory. Pustules may be opened with a tenotomy knife and emptied, the cysts may be emptied by curetting, their cavities being afterwards touched with pure carbolic acid, or silver nitrate. For these severe acnes also, the application of a strong exfoliating paste for two or three nights in succession is useful. This is repeated at intervals of about a week.

The nodular acne of women is intractable. There is more often than not some defect in general health; the patients are often constipated and easily tired; or their mode of life is not healthy. Vaso-motor instability is a factor in some of them. At the same time quite a number of them appear to be in good physical condition.

Œstrogenic drugs, especially stilbœstrol, have been used extensively in the treatment of acne, with some degree of success. In adequate dosage, however, they may provoke inter-menstrual hæmorrhage in girls or young women, and in males temporary gynæcomastia and loss of libido.

Staphylococcal toxoid or vaccoid have proved valuable occasionally.

Seborrhœic eczema is described with the erythemato-squamous dermatoses (*vide* p. 816).

ECZEMA

The term "eczema" is applied not to a single disease of constant ætiology but to a series of inflammatory reactions which succeed one another in stages, and which are caused by widely different pathogenic agents of external or internal origin. Clinically, eczema may be found associated with one or several of the following: erythema, vesiculation, weeping, crusting, desquamation, lichenification. Histologically the changes are constant in type though not in degree. In the epidermis they are intercellular œdema with splitting apart of the Malpighian cells, spongiosis, multiplication of the Malpighian cells, leading to increase in depth of the epidermis, particularly in the interpapillary portions, acanthosis, and failure of the Malpighian cells to keratinise in the normal way so that the superficial cells retain their nuclei, parakeratosis. These imperfectly keratinised cells lack the resistant quality of the normal horny layer and, becoming desiccated as the result of exposure to air, form the desquamated scale of eczema. In the dermis the changes are congestion, œdema, and more or less perivascular infiltration with small round

cells. Leucocytes are not found in the infiltrate in cases uncomplicated by secondary pyogenic infection.

Eczema is brought about by various internal and external agents. The older method of classification was purely descriptive, *e.g.*, squamous eczema, eczema rubra, eczema rimosum. This kind of classification is tending to become replaced by one based on the cause, though there still remain many cases in which this is either unknown or only partially known.

It is generally accepted that there is an external factor in very many cases of eczema ; in some this external exciting cause is obvious, *e.g.*, in industrial eczema. Sometimes it is no more than exposure to physical stimuli such as sunlight or cold winds. It is important to discover whenever possible the exciting cause, whether external or internal, and the predisposing causes.

External Causes.—*Traumatic Eczema.*—This is the result of scratching and may be due simply to pruritus or to some other pruritic disease such as scabies or pediculosis.

Parasitic and Microbic Eczemas.—Several of the ringworm fungi frequently provoke the eczema reaction on the feet and hands, while pyogenic infection is responsible for a large group of eczemas to be later described as infective dermatitis and impetiginous eczema. Pyogenic infection may also complicate eczema of non-infective origin.

Chemical Irritants.—These are so numerous that it would be useless to attempt to enumerate them. Moreover, their number is constantly increasing with the growth of industrial science. They may be divided into the following classes :—

1. Drugs : antiseptics such as lysol, formalin, mercuric iodide, iodoform, and others.

2. Substances derived from plants, such as primula obconica, " poison " ivy, chrysanthemums, daffodils, clematis, hops, teak, and many others.

3. Chemical substances used in all kinds of occupations, such as bichromate of potassium and ammonium used by engravers, tanners, furniture polishers, and others ; aniline dyes, especially paraphenylene diamine, used in the process of dyeing fur ; metolquinol and sodium hyposulphite by photographers ; soda by housewives ; lime and cement by builders ; sugar by sweetmakers ; dough and flour by bakers ; turpentine by painters.

Predisposing Causes of Eczema.—All these external agents provoke the eczema reaction only in predisposed individuals. Were this not so, almost everyone would develop eczema from time to time. Often the nature of this special disposition, which may run in families, is unknown, but sometimes it can be recognised. Among recognisable factors are excessive sweating and excessive dryness of the skin (ichthyosis) ; fair tender skins are more often attacked than those which pigment normally ; the resistance of the skin to external irritation diminishes with advancing years, and a high proportion of the cases occur from middle age onwards. Obesity is a common factor in the intertriginous eczemas. The devitalising effect of vascular hypostasis, particularly in relation to trauma and infection, is seen in the common varicose eczema. In recent years much stress has been laid on anxiety as a factor in eczema. It is doubtful whether nervous instability ought to be regarded as a predisposing cause, but there is no doubt that it is often an aggravating factor of great importance. The question of idiosyncrasy and allergy is discussed elsewhere.

Symptoms of Eczema.—In an acute outbreak of eczema or in an exacerba-

tion of a chronic eczema there is always in addition to more or less severe pruritus, which is a constant symptom, some degree of malaise and occasionally slight fever. The eruption itself is almost always polymorphic, some of the lesions exhibiting vesiculation, some crusting or weeping, or, in the healing stage, desquamation. Different stages of the reaction may be found in different parts of the same patch of eczema. An important objective symptom is œdema of the true skin. This gives to the lesions a somewhat firm consistency. The attack begins with a patch of erythema which quickly becomes sown with epidermal vesicles, which approach the surface, rupture, and discharge clear serum. The serum dries and forms crusts. If these be removed, tiny superficial pits are observed, which continue to discharge serum. The weeping stage usually lasts several days and is followed by a squamous stage. The desquamation may be slight and furfuraceous or abundant. On the palms and soles desquamation is usually specially abundant, or there may be marked thickening of the horny layer. The vesicular stage may be lacking from the first, which means that the primary vesicle has been too small to be seen with the naked eye. A patch of eczema may resolve completely or it may persist. Often chronicity is the result of persistent scratching ; in the course of several weeks an infiltrated patch is produced with marked epidermal thickening. In such a patch the normal furrows of the skin become accentuated. This stage is known as lichenification.

During the weeping stage the exudate often becomes infected with pyogenic organisms. This secondary infection or impetiginisation can give rise to folliculitis, boils, abscesses, adenitis, lymphangitis, sycosis, and blepharitis.

Distribution and Configuration.—Eczema has a predilection for exposed surfaces and for the large articular and other folds, but no part of the surface is exempt. There are, however, certain well-defined varieties which merit separate description.

Eczema is usually disposed in irregular patches of variable size, but sometimes it occurs in coin-shaped plaques, often found on the forearms, backs of the hands and legs, and not infrequently on other parts of the body. This type has received the descriptive name of *nummular eczema* or *papulo-vesicular eczema.* The lesions begin usually as a single large vesicle situated on a papular base. Other similar vesicles quickly appear in the immediate neighbourhood. In the course of days a confluent, rather firm plaque is formed. With rupture of the vesicles a superficial confluent crust forms. The eruption comes out in crops and is frequently associated with patches of the ordinary irregular type. Nummular eczema is recognised as occurring commonly in connection with either a long-standing chronic patch of eczema, *e.g.*, varicose eczema, or with some local septic lesion of the skin, *e.g.*, a whitlow, boil, discharging sinus, or infected wound. In many cases, however, no primary sensitising focus can be found in the skin or elsewhere.

Dysidrosis or Cheiropompholyx.—The eruption which was first described by Tilbury Fox begins in the form of epidermal vesicles upon the palms and soles and lateral aspects of the fingers and toes. Owing to the thickness of the horny layer in these regions the vesicles seldom rupture, and feel like lead shot in the skin. Occasionally they rupture, particularly on the fingers, but as a rule they are absorbed in the course of some weeks and give place to desquamation. Generally this is very abundant, and regeneration of the horny epidermis takes place slowly in the course of three or four weeks.

During the eruptive stage itching is a pronounced symptom. Dysidrosis occurs almost exclusively in subjects with hyperhidrosis of the palms and soles ; it is a recurrent disease and is comparatively common in the warmer months. In some subjects, however, it recurs at more or less regular intervals irrespective of temperature. Tilbury Fox believed that dysidrosis was caused by blockage and acute dilatation of the sweat ducts, but histological studies have shown that the primary lesion is an eczematous vesicle. It is evident, however, that the disease is related to a disturbance of the sweat apparatus, the precise nature of which is at present undetermined. True dysidrosis has to be differentiated from a number of eruptions of varying ætiology with which it is objectively identical. Thus there is a dysidrosiform fungus infection of the soles and palms caused by ringworm infection, and it is quite often associated with eczema on other parts of the body, particularly seborrhœic eczema. An intractable dysidrosiform eczema of the hands and feet may occur as a complication of scabies in children. The differential diagnosis, particularly of a first attack, may be difficult, and it is essential, when the feet are attacked, to exclude fungus infection by microscopical examination.

Keratotic Eczema of the Palms and Soles.—This type occurs most commonly in elderly subjects. It is accompanied often by deep fissures in the natural folds.

Hypostatic and Varicose Eczema.—This type, due to vascular stasis, is often found over the malleoli, about the ankles, feet, and on the legs, chiefly in heavy subjects with or without varicose veins. An area of vesicular, squamous, or lichenified eczema may be found which frequently becomes impetiginous. Similar areas of chronic eczema are found on the legs in elderly subjects in the absence of varicosities, and are to be attributed both to hypostasis and senile devitalisation of the skin. In some cases the whole of the leg may be involved.

Impetiginous Eczema and Infective Dermatitis.—In neglected impetigo, particularly of the scalp, nares, labial commissures, and ears, chronic eczema frequently supervenes. The skin becomes sensitised to the infecting organisms or to the products of tissue disintegration, and a simple pyodermia becomes transformed into a pyogenic eczema, or the infection may be the result of recent measles, whooping-cough, or other infection involving the nose and throat. There is a tendency for the process to extend to the intertriginous folds, especially the umbilicus, axillæ, and the genito-crural region. In acute cases the scalp, ears, and post-auricular folds pour with serum. This is followed by a crusted stage, and finally by a stage with constant desquamation. Sometimes the hair is suddenly shed, either partially or completely, during an attack, and following this event recovery is usually rapid. Relapses may take place at intervals throughout life.

Compound fractures are sometimes complicated by eczema, particularly when the limb has been encased in plaster. Beginning at the site of fracture, it extends gradually to form a sharply marginated area of eczema of varying dimensions, sometimes involving the greater part of the limb. Recovery takes place satisfactorily in the absence of residual necrosis of bone. The same change is met with in relation to osteomyelitis, chronic otorrhœa, and any other persistent pyogenic infection involving the skin.

Intertriginous eczema of the large folds is often due primarily to pyococcal infection : for this, excessive sweating and sometimes obesity are often partly

responsible. This type of eczema is often very persistent, far more so than the somewhat similar eruptions due to *Epidermophyton inguinale* and *Oidium albicans*.

Seborrhœic Eczema.—This is described elsewhere (*vide* p. 816).

Eczema caused by External Irritants.—Some of the chemical substances capable of causing eczema have been already mentioned. The lesions do not differ from those of eczema due to other causes, and are found primarily on parts exposed to the irritant, usually the forearms, wrists, and hands, and sometimes the face and neck. The eruption may be vesicular or squamous, fissured, secondarily impetiginised in parts or lichenified, and disposed more or less uniformly in the areas affected, or in nummular or irregular patches. There is a tendency to spread beyond the regions primarily affected, *e.g.*, to the face and neck and the flexures. The extension is thought to be due to some sensitising substance derived from the initial focus.

The substances commonly responsible for occupational eczema are irritating only to susceptible individuals. Subjects with hyperhidrosis or ichthyosis, or with fair tender skins, are more liable to become sensitive than are those with normal skins. Susceptibility is generally acquired after prolonged contact with the irritant substance ; or, expressed in another way, the skin after sustaining for years the impact of some damaging substance, eventually breaks down ; this often occurs after many years, and at an age when the natural resistance of the skin is diminishing. Far more rarely sensitivity is exhibited almost immediately (idiosyncrasy). In either case the disease is cured either rapidly or sometimes, particularly in the former group, with considerable difficulty after cessation of contact with the irritant substance. Eventually the skin may appear to be normal, but re-exposure invariably excites a recurrence. Moreover, the individual has often acquired a tendency to develop eczema on exposure to chemical irritants other than those which he has previously handled.

The frequent employment of the term "dermatitis" for the eczema reaction has given rise to a certain amount of confusion, and no general agreement appears likely to be reached on this point in terminology. It has been suggested that when the cause is a known irritant, whether it reaches the skin from outside or by the blood stream, the case should be labelled dermatitis. Thus there are occupational or professional dermatitis ; dermatitis venenata where the irritant is a plant ; toxic dermatitis ; infective dermatitis ; solar dermatitis, etc. This leaves for eczema only certain idiopathic types, such as nummular eczema. This is a simple way of indicating that the exciting cause is known. But it is necessary to recognise that the term "dermatitis" thus applied includes all types of inflammatory response to an irritant, and these are not always eczematous. Thus the reaction to sun or wind may be simply erythema followed by peeling, or it may, in certain cases, be eczematous, and the same variations may be met with in relation to other irritants.

Thus it would be correct to describe the eczematous cases as eczema—occupational, infective, solar, etc.—and the non-eczematous as dermatitis. But this would lead to difficulties in certification of unfitness for work, since under the Workmen's Compensation Act any reaction of the skin provoked by industrial irritants has to be certified as "dermatitis."

The difficulty can be overcome by adding to dermatitis the qualifying term "eczematous" in the appropriate cases.

Disseminated Neurodermatitis.—Long-continued eczema, of whatever origin, is often followed by several large or small areas of lichenification. Owing to the repeated scratching to which these intensely pruritic areas are subjected, they may persist almost indefinitely. As its name implies, there is often in this condition a background of nervous instability.

Infantile Eczema and the Eczema-Asthma Complex.—There are three well-defined types of infantile eczema: (i) primary eczema of the face; (ii) eczema of the scalp of infective origin; (iii) eczema derived from napkin erythema.

Primary Eczema of the Face (Atopic Eczema).—This occurs at any period from the second month onwards, and usually affects the forehead and cheeks but spares the nose and circumoral area. Other parts of the body are also often affected. The eczema may take the form of a vesicular and weeping eruption in fat children, but is often dry and scaly in marasmic infants. The scalp is usually spared at first, but is generally involved eventually by direct extension of the process. The condition may clear up quickly, but is more often intractable. It may disappear at the end of the teething period. When it persists, it tends largely to leave the face and to appear predominantly in the flexures in the form of lichenification. In this phase of the condition, which is known usually as Prurigo of Besnier, the lesions are determined almost entirely by scratching. It may persist with remissions and exacerbations to puberty or into adult life, and even after disappearance in infancy may recur in later years. About 30 per cent. of the cases develop asthma or chronic bronchitis, usually from three years of age onwards; about 20 per cent. have ichthyosis. When the disease occurs in older children or in adults, the constant friction and consequent thickening of the skin of the face produces a characteristic rigid aspect. Accentuation of the normal furrows about the mouth is often striking in these older subjects, and this, combined with an earthy complexion, which is equally characteristic, is a safe guide to the correct diagnosis. These patients are often sensitive to one or more allergens, such as foodstuffs, animal emanations, and pollens, but although these may give rise to such temporary symptoms as sickness, urticaria, swelling of the mouth, or hay fever, they are evidently not responsible for the constant itching and prurigo.

Infantile Eczema of the Scalp.—This type, which begins at about the same period as the preceding, appears usually to originate from pityriasis of the scalp. The scales are sometimes found on examination to be infected with the pityrosporon. In some cases it is possible that the infection may be transmitted from the parents. The eczema may be vesicular, crusted, or squamous, and tends to extend to the post-auricular grooves, the neck, and the face, and sometimes to other parts. It is more amenable to treatment than atopic eczema.

Intertriginous Eczema.—This usually occurs primarily in the napkin area as a diffuse erythema affecting the convex surfaces of the buttocks and thighs, and is due to the irritating action of the urine, which is nearly always ammoniacal. This change is caused by the action of a bacillus found in the fæces which has the property of converting urea into ammonia. Although a simple erythema to begin with, the condition tends to spread into the inguinocrural and intergluteal folds and to become eczematous. The eczema may become widespread.

Treatment of Eczema

The subject is too large to be dealt with here in any but the most summary fashion. The treatment of eczema is greatly facilitated if the cause can be accurately ascertained and eliminated. In certain cases rapid cures are often achieved by the successful treatment of a focus of origin, such as a patch of lichenification, a varicose ulcer, or any chronic septic lesion in the skin; in others by the discovery of an unrecognised external factor, such as a plant to which the individual is sensitive; or by cessation of work in eczema of occupational origin. Enough has already been said regarding the causes of the various types of eczema to indicate the manner in which a given case should be investigated. Of equal importance is the alleviation of symptoms by local and general measures.

Local Treatment.—There are certain principles to be observed, but the treatment must be elastic, varying according to the stage of the disease. Its object, which is to restore a damaged epidermis to its normal state, and particularly to assure that the horny layer is fully re-established, is best attained by careful protective measures.

In the acute erythematous and vesicular stages, in order to facilitate evaporation and drainage of serum and to cool an inflamed surface, it is advisable to use simple watery lotions, watery pastes, or oily liniments containing no antiseptic. Calamine lotion, lead lotion, or calamine liniment may be used for this purpose.

In impetiginous and crusted eczemas accumulated crusts must be removed; this is often best accomplished by boric compresses or starch and boric poultices, or it may be advisable to soak off impetiginous crusts with a weak antiseptic, *e.g.*, solution of potassium permanganate 1 in 4,000, or silver nitrate 1 or 2 per cent. in water, before applying any other remedy.

Eczemas of infective origin, *e.g.*, those which complicate impetigo and many intertriginous eczemas of the ears, groins, submammary folds, etc., sometimes respond well to the application of a dye such as gentian violet $\frac{1}{2}$ to 1 per cent. in calamine lotion.

In the natural course of events the weeping stage of eczema is succeeded by desquamation (parakeratosis). At this stage protective creams and pastes which formerly would have been badly tolerated are indicated. These replace in part the fat which is lacking in the parakeratotic cells.

When, as a result of repeated scratching, lichenified and indolent infiltrated patches of eczema are produced, it is usually advisable to add one of the reducing agents such as ichthyol, tar, or lenigallol in varying proportions to a paste or cream (*vide* p. 844). To such patches X-rays applied in fractional doses are often of the greatest value.

General Measures.—In the acute stage of eczema there is no general measure more valuable than complete mental and physical rest. The digestion and excretory functions must receive careful attention.

There are no hard and fast rules regarding diet in eczema; overfed obese subjects benefit from a weight-reducing regime; equally malnutrition when present in eczema should receive appropriate dietetic treatment. Alcohol should be forbidden. In atopic eczema diet should be free from allergens to which the patient is found to be sensitive.

Treatment by Internal Remedies.—The eczematous reaction results from numerous causes, and there is no single remedy capable of universal

application in its treatment. Drugs are of value only in exceptional cases. The daily intravenous injection of a 10 per cent. solution of sodium or strontium bromide in physiological saline is of value in reducing œdema and weeping in cases of widespread eczema but not in localised cases. Autohæmotherapy, the injection of 10 to 15 c.c. of the patient's own blood into a muscle, about every five days, meets with success in a number of widespread but not localised eczemas. In contrast to other varieties of eczema atopic eczema is sometimes kept under control by the antihistamine drugs, such as Antistin or Anthisan.

ERYTHEMATO-SQUAMOUS DERMATOSES

A number of dermatoses consist essentially of dry scaly erythematous spots and patches. Among these are certain cases of ringworm infection, lupus erythematosus, the type of streptococcal infection known as pityriasiform impetigo, some irritant and toxic eczemas, and seborrhœic eczema. Under the heading of erythemato-squamous dermatoses are also included three unrelated dermatoses of unknown cause, namely pityriasis rosea, psoriasis, and the parapsoriases. For a description of the last named the reader is referred to works on dermatology.

Seborrœhic Eczema

Unna assembled under the name of seborrhœic eczema a group of eruptions which though differing from one another in some respects had certain characteristics in common ; there were also transitional forms linking the different members of the group. He used the term seborrhœic because the principal number are found in seborrhœic subjects, and on parts in which sebaceous secretion is most abundant. Nevertheless the term is not accepted universally, the French school, particularly, rejecting the role of seborrhœa in their genesis. Darier, rejecting seborrhœa as an essential factor but recognising a close relationship with eczema, named them eczematides. Confusion has also arisen from a tendency to apply the term seborrhœic eczema loosely to any eczema occurring in seborrhœic subjects, and to eczema of whatever origin attacking the scalp or the large folds. Using the term in its original restricted sense, the members of the group seborrhœic eczema or eczematides are six in number.

They occur most often though not invariably on a seborrhœic or kerotic background, and dandruff is usually abundant.

Seborrhœic Eczema of the Scalp.—Dandruff or pityriasis capitis is probably universal, though more abundant in some, usually seborrhœic, subjects than in others. The scales are not dried sebaceous secretion as they were believed to be at one time, but desquamated horny scales. Dandruff gives rise to a certain amount of itching, and it is sometimes associated with inflammation. The scalp is generally dry, red, and scaly, but sometimes there is serous oozing. The same changes often take place in the eyebrows, and along the margins of the eyelids (seborrhœic blepharitis), while there is also a tendency for it to spread from the scalp to the ears and on to the neck ; dry scaly areas are commonly found on the face. Boils, impetigo, and fissures occupying the post-auricular folds or the corners of the lips or the nares are common complications.

The Figurate Type.—The sites of election are the centre of the chest and back; it is the most common variety, and it consists of dry scaly patches of petaloid outline. The initial lesion is a dry red papule of about the size of a small pin-head, or a group of papules. By the addition of fresh papules the lesion spreads centrifugally, while those in the centre disappear, leaving a fawn-coloured scale, greasy to touch. These petaloid lesions eventually become almost stationary and persist if untreated for months or years.

Subacute Follicular Type.—This consists of an acute or subacute follicular papular eruption occurring chiefly on the chest and back. The lesions arise in the course of a few days and do not in the early stage exhibit the figured patches of the dry type, although eventually some such patches may be formed by confluence and involution of the papular lesions. This variety occurs commonly in subjects with hyperhidrosis and in those who work in warm rooms or wear woollen or flannel garments next to the skin. The same factors predispose also to the production of the figured type. The eruption is irritable.

Pityriasiform Type.—The lesions are dry, superficial, scaly patches which resemble somewhat the lesions of pityriasis rosea. They have an acute onset and occur quite often on the limbs as well as on the chest, back, and abdomen. This type may be accompanied by vesicular eczema of the palms and soles or of the flexures.

Psoriasiform Type.—Seborrhœic dermatitis seldom resembles psoriasis, but occasionally lesions practically indistinguishable from psoriasis are produced. They occur chiefly along the extensor aspects of the limbs and occasionally on the chest and back. They consist of irregular patches with lamellated scales, which sometimes, though not always, spread centrifugally and clear in the centre like the figured patches.

Generalised Seborrhœic Dermatitis.—In this rare condition the individual follicular papules coalesce to form large desquamating areas covering a great portion of the surface.

Ætiology.—The scales of dandruff are found, on staining, to contain groups of spores of varying shapes—oval, round, dumb-bells, or gourds; this organism is a fungus, known as the Bottle bacillus, spore of Mallasez, or pityrosporon; its disposition in the scales is similar to that of microsporon furfur in pityriasis versicolor, and it is widely believed to be the cause of the desquamation. The pityrosporon has been cultivated, and its implantation on the lightly scarified skin has been followed by the appearance of lesions like those of the figurate eczematide. The writer and J. M. H. Macleod obtained similar results by implantation of a monilia grown from the scales of dandruff. Unna thought that dandruff and seborrhœic eczema might be due to a combination of two organisms, the Bottle bacillus and what he called the morococcus, now assumed to have been staphylococcus albus. On the whole, it seems likely that the indolent petaloid variety of members of the group may be due to the growth on the skin of the pityrosporon.

It has been held by Ravaut that the more acute and widespread types represent an allergic reaction to infection by yeast-like organisms.

The tendency appears to be to look for infection as the direct cause, and a variety of other factors, including seborrhœa, as predisposing causes. In this latter respect the problem is the same as that presented by eczema in general.

Treatment.—The dry figured type of seborrhœic dermatitis is easily cured by the application of pastes and ointments containing sulphur. For the more acute types sulphur is usually too irritating. Pastes and creams containing solution of tar or ichthyol are generally found valuable. The general management of the more acute cases is similar to that of eczema due to other causes.

Pityriasis rosea

The eruption consists of two types of lesion :—

1. Pink squamous macules, irregular in shape and varying in size from a pin's head to a lentil or larger.

2. Circumscribed oval macules, generally described as medallions. The periphery of the lesion is often pink and slightly raised, while the centre is fawn-coloured. The scales are often arranged as a collarette just inside the peripheral pink zone. Moderate pruritus is usually present.

Usually the generalised eruption is preceded for several days by a single medallion larger than those which are to follow. This is called the *herald patch*. The disease runs a self-limited course and clears up within two months. Slight enlargement of the lymphatic glands may be present, and it seems probable that the condition is caused by an infective agent. Recurrences are very rare.

Treatment.—Pityriasis rosea is better left untreated. To allay irritation, when present, phenolated calamine lotion may be used. Ointments are badly tolerated.

Psoriasis

This important disease is one of the commonest in dermatology and one of the most intractable. It occurs in the form of red scaly spots, patches, and even sheets of the greatest possible variety of shapes and sizes. The terms "guttate," "nummular," "discoid," "gyrate," "circinate," "rupioid," and others are descriptive names applied to the numerous varieties of the disease. The characteristic lesion consists of a red patch or spot covered with dry lamellated scales which are heaped up on one another to a variable degree, and when gently scraped with a curette exhibit a silvery lustre. Complete removal of the scaly portion of the lesion exposes a red glistening surface upon which soon appear fine bleeding points. Psoriasis appears particularly upon prominences and on other parts which are naturally subjected to trauma ; thus the scalp is rarely spared, and the elbows and knees are almost invariably affected. The extensor surfaces of the limbs suffer more frequently than the flexor surfaces, but no part of the body is exempt. The exposed surfaces are less often attacked than the covered parts. The eruption may be extremely profuse or limited to a few spots. The scalp may be affected alone, or the nails alone, or the palms and soles, or the elbows and knees. There is a strong tendency to symmetry and uniformity of lesion.

Psoriasis of the Scalp.—This is frequently mistaken for seborrhœic dermatitis. On the scalp psoriasis generally occurs in the form of well circumscribed patches with marked heaping up of scales on the surface and with intervening normal areas of scalp, while seborrhœic dermatitis is usually distributed over the whole scalp, and the scales are less lamellated.

Intertriginous Psoriasis.—This type affects particularly the articular and other folds, and is usually disposed in large flat patches covered with crusts

rather than scales, often fissured and sometimes weeping. This variety, which closely resembles eczema, is rather frequent in elderly and obese subjects: the deep red colour and sharp outline of the plaques are sufficient to distinguish them from eczema.

Exudative Psoriasis.—Psoriasis may be disposed in extensive red sheets constantly desquamating, sometimes weeping in parts, and covering a considerable proportion of the body.

Psoriasis of the Nails.—This may exist alone. The nails are pitted, longitudinally or transversely striated, and thickened to a varying degree. They may be partially separated from their beds.

Psoriasis of the Palms and Soles.—This exists usually in company with psoriasis elsewhere either in the form of well circumscribed hyperkeratotic plaques or of a confluent area involving the whole or the greater part of the palmar surface. It is not usually irritable.

Pustular Psoriasis.—This extremely intractable condition occurs almost invariably on the palms and soles, and consists of red scaly areas of variable dimensions and shape studded with intra-epidermal yellow pustules of about the size of a small pin's head. The pustules dry up in the course of a few days and are at first replaced by small yellowish brown spots consisting of dead epithelium and leucocytes, which eventually separate to leave shallow pits bounded by a detached horny collar. Fresh pustules continue to appear both in the affected areas and in the neighbouring healthy skin.

Arthropathic Psoriasis.—Psoriasis is commonly associated with rheumatism of all degrees, ranging from slight stiffness in one or two joints to severe rheumatoid arthritis; the psoriasis is in such cases often extensive and inveterate.

Evolution and Prognosis.—Psoriasis begins usually as an acute attack affecting the limbs and trunk. The lesions are usually, though not invariably, of the guttate type in the first attack. Thereafter, one attack succeeds another, with intervals of comparative, though seldom complete, freedom. While exacerbations and remissions are the general rule, a certain number of patients have only a few lesions, often on the points of predilection, which last for years. Under treatment psoriasis may sometimes be made to clear up entirely. With the disappearance of the spots, depigmented patches are generally left, particularly after treatment with chrysarobin; sometimes, however, pigmented patches remain for months. No case can be regarded as permanently cured.

Ætiology.—Psoriasis may occur at any age, in both sexes, in all races, and in all countries. First attacks are most common at school age and adolescence, but are not very uncommon in old age. Though the precise causes are quite unknown certain ætiological factors are established, of which the most important is heredity. The exciting factors are variable or apparently non-existent in many cases. Pregnancy is an exciting cause in some cases, while others are only free from psoriasis during pregnancy and lactation. Trauma is a well-recognised cause, and the occurrence of psoriasis upon prominences is an expression of this factor. The first attack of an acute guttate psoriasis is very often preceded by tonsillitis. On the other hand, psoriasis may clear up during a severe febrile illness. The seasons and climate have an influence on its production; it is said to be uncommon in the tropics. In the present state of knowledge perhaps the most rational view is that there is an inherent fault in the skin of some individuals who have an innate

predisposition, often obviously inherited, to react in the form of psoriasis to various stimuli, internal and external.

Treatment.—This consists mainly in the application of various remedies which have proved capable of curing the condition temporarily. The first stage of local treatment consists in the removal of the scales. This is done by softening for several days with salicylated olive oil or with a simple ointment containing salicylic acid, and is further facilitated by the daily use of soap and warm water, using a nail brush. A preparation containing one or other of the reducing agents is then used. Solution of coal tar, crude tar, oil of cade, chrysarobin, dithranol, pyrogallol, and resorcinol, or a combination of two or more of these drugs, are those most frequently employed, of which the last two are the most effective, though dirty and sometimes badly tolerated. Dithranol, a more active but cleaner derivative of chrysarobin, is now often used. X-rays are often used to clear up obstinate patches, but although a clean method and usually successful, this form of treatment is unsatisfactory on account of the risk of damaging the skin. Thorium X is somewhat less effective but can be used with safety. The mercury vapour and carbon arc lamps have been used successfully in some cases as local treatment, especially in combination with crude coal tar.

There is no known rational or reliable general remedy. Arsenic by mouth is rightly used less than formerly ; it is often temporarily effective in suitable cases, but its prolonged or too often repeated use has sometimes led to degenerative change in the skin, and occasionally to carcinomata. Otherwise temporary success has been claimed from time to time for a long list of remedies, *e.g.*, the intramuscular injection of whole milk, sulphur in oil, turpentine, and salvarsan derivatives ; by mouth, salicin, iodine, thyroid extract, sulphur, calciferol in large doses combined with exposures to ultra-violet light, and many others. In fact we have to rely chiefly on correctly applied local treatment, which in extensive or severe cases is best carried out in hospital and combined with rest.

ALLERGY AND DISEASES OF THE SKIN

The term " allergy " (altered reaction) was coined by Von Pirquet to denote the alteration in degree of sensitivity of the skin to Koch's old tuberculin which he observed during the various phases of tuberculosis. It was heightened during some phases and diminished or absent in others, such as advanced pulmonary tuberculosis. From that time the term has been employed to cover an ever-increasing field, including some conditions which appear to be closely related to anaphylaxis.

At the present time the term is generally held to imply reactivity to an agent of any kind which at some previous time provoked no reaction at all or a slighter one.

Coca classifies the manifestations of allergy as follows :—

1. Serum sickness. 2. Atopy. 3. Drug allergy. 4. Bacterial allergy. 5. Dermatitis—sensitivity to external irritants.

Coca coined the term " atopy " to denote a special liability to develop sensitivities of various kinds that often runs in families, and under atopic diseases he includes atopic eczema, asthma, hay fever, and urticaria. Among

the manifestations of the atopic state there is a strong tendency to develop sensitivity to various foodstuffs, animal emanations, pollens, and even house dust.

The presence of such hypersensitivity can be demonstrated by the passive transfer test (Prausnitz-Küstner reaction). A drop of the serum of a sensitive subject is injected intradermally into a normal subject. Within about half an hour the site of injection will exhibit sensitivity to an extract of the substance to which the patient is sensitive when applied as a skin test, by scratch test or intradermal injection, or if a food, when taken by mouth. This reactivity becomes more pronounced after twenty-four hours and the sensitised patch of skin remains sensitive for several weeks.

Sensitivity to foods is manifested either by alimentary intolerance, sickness, or diarrhœa, by swelling of the lips or face, or by generalised erythema or urticaria. It has been too readily assumed that infantile eczema is the result of hypersensitivity to food. This condition appears and persists in infants on a pure milk diet in whom sensitivity to milk is absent. Most of them give a positive reaction to egg, even when no egg has been given at any time, and the strict avoidance of egg does not usually terminate the eczema. The exact mechanism of this type of atopy has not yet been clearly demonstrated.

Urticaria

Symptoms.—This common condition is characterised by the development of transient wheals. The first objective symptom is a patch of erythema, which is quickly followed in a typical lesion by formation of a central wheal surrounded by a peripheral erythematous zone. The lesions may be round, oval, or of irregular outline; they are of all sizes, and may occur on any part of the body. They are invariably accompanied by severe itching, which is greatest in the erythematous or even the pre-erythematous stage of the lesion. The swelling slowly subsides, to disappear as a rule within a few hours. An acute attack may be accompanied by transient slight fever.

Varieties.—Modifications in the objective features of urticaria have given rise to special names. In giant urticaria or angioneurotic œdema the lesions are large œdematous swellings involving the subcutaneous tissue, and often the mucous membranes, particularly of the mouth, and occasionally of the pharynx and larynx. The condition may or may not be accompanied by the common type of wheal.

Bullous urticaria, in which some of the lesions consist of large bullæ, is rare. Extravasation of blood into the lesions has given rise to the name hæmorrhagic urticaria; this also is uncommon.

Urticaria due to Heat.—This not very common variety has been studied by R. T. Grant and Bruce Pearson. It appears only as the result of heat or emotion. Strenuous exercise, hot baths, or emotional excitement are followed by a generalised crop or small urticarial spots which persist for a few hours and do not reappear until the patient is again subjected to the same conditions. A severe attack is followed by a short refractory period during which exercise may be taken with impunity. Most of the subjects have been young women.

Urticaria due to Cold.—After exposure to cold air or cold water the part of the skin so exposed becomes the site of an urticarial eruption or patchy

erythema similar to that caused by heat. Occasionally the two conditions are found in the same subject.

Dermographism.—In this a wheal is readily provoked by light friction of any kind such as pressure of a corset or friction of a towel. The urticarial reaction so provoked occurs only at the site of friction and is transient. Many of the patients are more or less dermographic permanently but are not greatly inconvenienced by it except during phases of increased intensity. These occur often for no demonstrable reason, though emotional disturbance is thought to be sometimes responsible for exacerbations. A noteworthy degree of dermographism is rarely demonstrable in other varieties of urticaria.

Course and Prognosis.—A proportion of urticarias are due to the ingestion of some drug such as penicillin or aspirin, or foodstuff, to which the individual is sensitive, or to partially decomposed food. These cases seldom persist for more than a few weeks. There are, however, a great number of chronic urticarias in which it is impossible to discover any specific cause, and these may persist for many months or even years with occasional remissions. Angioneurotic œdema or giant urticaria is a particularly persistent type.

Ætiology and Pathogenesis.—The urticarial reaction may be called forth by numerous causes of external or internal origin. The sting of a nettle, and the bites of mosquitoes, fleas, bugs, and other insects arouse urticarial reactions of varying intensity according to individual susceptibility. Of internal causes the best known are drugs and foodstuffs to which the individual is susceptible. Fish, egg, pork, decomposing food of any kind, and strawberries are among the most frequent examples. Hydatids and intestinal worms are occasional causes.

Urticaria may also be caused by toxic products developed in the body. Thus it may occur in pregnancy and in the course of disease. Emotional instability is met with frequently in chronic urticaria and is widely held to be a relatively common causal factor. In the majority of chronic cases, however, it is impossible to discover a cause.

The researches of Lewis and Grant have thrown light on the mode of production of urticaria. It has been shown that a lesion identical with an urticarial wheal may be produced by pricking into the skin a drop of a solution of histamine of 1 in 20,000 dilution. The reaction so produced is threefold in nature: first, capillary dilatation due to the direct action of histamine on the capillary wall, then an areolar flush due to reflex dilatation of arterioles round the puncture, then increased permeability of the capillary wall leading to œdema, *i.e.*, wheal formation.

The mechanism of urticaria caused by sensitivity to food has been shown to be related to anaphylaxis by the study of the passive transfer reaction. It is assumed that in the affected tissues there are fixed antibodies and that the interaction of such antibodies with the foodstuff gives rise to an explosive reaction with a liberation of histamine. In urticaria due to heat the mechanism has been shown also to be due to the liberation of histamine. This type can be inhibited in an area such as an upper limb by blocking the cutaneous nerves. It can also be brought on by the administration of doryl (acetylcholine). R. T. Grant and Bruce Pearson have shown that first the para-sympathetic nerves are stimulated by heat with the liberation of acetylcholine and secondarily histamine, presumably in these subjects in excess. Exercise may produce in them a histamine effect of such severity as to give rise to marked pallor, a rapid pulse, and a fall in blood

pressure. Urticaria due to cold can be passively transferred to a normal subject by the intradermal injection of the serum of a cold-sensitive subject. The site of the skin so treated if immediately exposed to cold, *e.g.*, from a cold water tap and afterwards warmed, develops a wheal. It is supposed that a dermolysin exists in the blood of such subjects which, when the skin is exposed to cold, becomes fixed to the cutaneous cells, lysin them on re-warming. This type of urticaria is sometimes found in subjects with paroxysmal hæmoglobinuria. In severe chronic urticaria, especially giant urticaria, the presence of a whealing substance in the circulation can be readily demonstrated; it is absent during remissions.

Treatment of Urticaria.—Success in the treatment of urticaria depends chiefly upon elimination or avoidance of the cause. When the cause is definitely known to be a food such as shell-fish, egg, or strawberries, the prognosis is generally good, although an attack may be prolonged for a few weeks.

Of treatment by drugs, calcium lactate by mouth or calcium chloride injected intramuscularly have been used extensively, but with disappointing results. Subcutaneous injections of 5 to 10 minims of adrenaline hydrochloride have been used successfully for the immediate relief of symptoms and are valuable in angio-neurotic œdema, but the effect is transient.

In the past few years a series of drugs spoken of as anti-histamine drugs have been developed. Those in common use at the present time are Benadryl and Pyribenzamine, introduced in America, and Neoantergan Malleate (Anthisan) and Antistin, developed in France and Switzerland. They neutralise histamine quantitatively in some way; it has been suggested that they compete with histamine for a site of action or receptive substance in the same way as para-aminobenzoic acid competes with the sulphonamides. They are given chiefly by mouth and the dose in the case of Benadryl is 50 mg. three or four times daily; more than twice that amount of Anthisan or Antistin may be given. The therapeutic effect in urticaria, relief of itching and flattening of wheals, becomes apparent within a few hours. In urticaria due to food or a drug such as penicillin it is often possible to mask the attack almost completely until it has come to an end naturally.

Chronic urticaria, on the other hand, invariably relapses when the drug is discontinued. These drugs are cerebral depressants and Benadryl, the first to be applied therapeutically on a large scale, is the most toxic of the series. The toxic symptoms to which they give rise are chiefly drowsiness, restlessness, giddiness, dryness of the mouth, nausea, and headache. These may be brought to an end by the injection of histamine phosphate in doses of 0·5 mg. They pass off spontaneously within a few hours.

Treatment of urticaria by local measures is of secondary importance. Lead or calamine lotion with the addition of phenol, 10 gr., or liquor picis carbonis 1 drachm to the ounce of lotion serves to diminish pruritus.

Papular Urticaria

This common condition occurs chiefly in infants and young children. The lesions consist of firm papules surrounded by a halo of erythema. Often the central papule is surmounted or even replaced by a vesicle or bulla. The eruption may occur on any part, and may be mild or of extreme severity. It is always markedly pruritic. An attack normally lasts about three weeks but

may be prolonged for months. The condition usually dies out at the age of four or five years, but exceptionally it may recur at intervals until puberty or later. In persistent cases the lesions become aggregated on parts naturally subjected to trauma, and particularly along the extensor aspects of the limbs and on the buttocks. There is in such cases a close resemblance to Hebra's prurigo, to which disease papular urticaria is believed by some to be related.

Ætiology.—In the majority of cases of papular urticaria in children no cause can be discovered, though rarely it may be recognised as a definite article of diet. Attacks occasionally occur during the eruption of a tooth. Intestinal worms are held to be responsible for some cases. R. Hallam observed that the eruption invariably cleared up on admission to hospital and that a relapse often followed the return of the patients to their homes. Attempts were made to provoke a recurrence while in hospital by various dietary restrictions and excesses, by giving the patients food prepared at their homes, by making them sleep in their own bedclothes, and by sprinkling dust from the home in the bed. All failed completely. Papular urticaria is not common in adults, and its cause, as in children, is obscure. It is occasionally a cutaneous manifestation of lymphadenoma and rarely of leukæmia. Hallam's investigations suggest that environment may be the important factor.

Treatment.—This consists of the avoidance of the cause in the exceptional cases in which it can be recognised. A change of locality will often bring about a cure in chronic cases, and particularly admission to a hospital ward. The anti-histamine drugs are ineffective. For local treatment anti-pruritic lotions and powders may be used. Cotton or silk garments should be worn next the skin. Secondarily infected lesions should be treated by local antiseptic remedies.

LICHEN PLANUS, LICHEN SIMPLEX, AND LICHENOID ERUPTIONS

Lichen Planus.—This common eruption is composed mainly of small dry papular elements of polygonal outline of about the size of a pin's head or somewhat larger; the surface is flat, the centre often slightly depressed, umbilicated, and when viewed at the right angle it is seen to have a brilliant surface. At first pink, the colour later becomes characteristically violaceous. Observation with a lens reveals, beneath what appears to be a translucent horny covering, opaque white streaks, known as Wickham's striæ, disposed irregularly in the papule, but sometimes radiating like the spokes of a wheel from the central umbilication.

Lichen planus, however, exhibits a good deal of polymorphism, and in addition to the characteristic papules there may be: (i) groups of horny follicular lesions, often disposed about one or more flat papules (lichen planopilaris); (ii) large elements found most often in the lower extremities, but occasionally on other parts as well, hard and warty, raised well above the surface, or flat with a rough horny surface; (iii) in the opening stages of an acute attack the lesions may be simply erythematous patches and spots bearing a close resemblance to pityriasis rosea; among them the characteristic papules appear shortly. (iv) In the rare lichen planus of the scalp the lichen

pilaris type of lesion is usually found in groups ; these are sometimes replaced finally by patches of cicatricial atrophy ; similar areas are occasionally found in the axillæ. (v) In the mouth, particularly on the buccal mucous membrane (in which lesions are found in approximately half the cases), lichen planus appears as opaline milky blue patches, or most often as a bluish-white reticulation, resembling the white streaks seen in the papules. (vi) Rarely, in very acute attacks, blisters may develop in some of the papular lesions. (vii) Scar-forming papules are also relatively rare. (viii) Annular lesions are comparatively common.

Configuration and Distribution.—The papules may be discrete and very widespread, covering a large part of the surface, and in some parts confluent. The disease may, however, be localised, *e.g.*, to the buccal mucous membrane, to the genitalia, to the front of the wrists and forearms, to the lower extremities, or to a combination of a few or several of the above common localities. The papules may be arranged partly in rings ; one or more papules are frequently surrounded by a group of horny follicular papules (lichen plano-pilaris). The face and other uncovered parts are generally spared, though not always, the lips being attacked with some frequency and the eyelids less often. Lichen planus is often disposed in streaks along scratch marks.

Symptoms.—There may be no subjective symptoms, but usually there is some irritation, and occasionally this is extremely severe. Patients are often unconscious of lichen planus in the mouth, but there is occasionally some soreness.

Course and Prognosis.—The course is irregular but almost always slow. Acute widespread attacks are likely to come to an end sooner than those of limited distribution. Hypertrophic lichen planus may persist for many months or even years. Relapses may take place, but they are generally less widespread and severe than the initial attack.

Ætiology.—Lichen planus is a disease of adults ; its cause is unknown. Nervous stress is often said to be one of the causal factors, but the type of patient and the history do not always confirm this belief. The not uncommon occurrence of identical lesions after the administration of organic arsenic, mepacrine, or gold would seem to suggest a toxic cause, but nothing is known of its nature or source.

Treatment.—In the absence of a known cause there is no known rational therapy. No local treatment except X-ray or Grenz-ray has any appreciable influence on lichen planus. Sedative applications may be used to allay itching when present. In acute attacks nothing is more effective than a period of complete rest. Severe itching in acute attacks is said to have been relieved on several occasions by lumbar puncture. Among empirical remedies that have achieved some success are mercury by mouth or by injection, arsenic (Acetylarsan, Enesol, Soamin), and vitamin B_1.

Lichen Planus-like Eruptions due to Gold or Arsenic.—The eruption may be purely of the lichen planus type, or it may be associated with erythrodermia ; sometimes it is seen when the latter begins to clear up, persisting for many months after all exfoliation has come to an end. When gold has been the cause, the lichen pilaris type of element is often a pronounced feature. The outlook is satisfactory, though involution takes place very gradually.

Tropical Lichenoid Dermatitis.—An eruption closely resembling the hypertrophic variety of lichen planus and usually of widespread distribution

occurred with some frequency in the Pacific and African theatres during the late war. This proved to be due to the cumulative effect of mepacrine.

Lichen Simplex Chronicus (*Widal*), **Pruritus with Lichenification** (*Brocq*).—In the absence of any preceding cutaneous lesion, particularly eczema, lichenification (*vide* p. 812) may be provoked by repeated rubbing or scratching of a pruritic area. The most common sites are the nape and sides of the neck in women; the inner aspect of the thighs, the scrotum, the extensor aspect of the forearms near the elbows, the legs, and buttocks. The lesion is generally an infiltrated plaque, smooth and burnished by repeated rubbing, and quadrillated by accentuation of the normal skin folds. Sometimes, however, there may be discrete papules somewhat resembling those of lichen planus but lacking the characteristic polygonal outline, bluish colour, and Wickham's striæ.

The chief causal factor appears to be nervous tension; this is practically always present and has to be taken into account when instituting treatment. The patients are often very responsive to small doses of superficial X-ray, to Grenz-ray or to Thorium X. Crude coal-tar, 10 per cent., in collodion and ether or White's tar paste are sometimes efficient remedies. Lichen simplex disappears slowly when rubbing is prevented by an occlusive dressing, *e.g.*, Unna's paste or several layers of Visco-paste bandage.

Lichenoid Eruptions.—A certain type of cutaneous eruption has been termed lichenoid, though unlikely to be confused with lichen planus. The most important examples are the lichenoid syphilide, tuberculide, and trichophytide. They have in common a localisation to the hair follicles and a disposition of the small acuminate papular lesions of which they are composed in irregular strands, patches, or even considerable areas, forming sometimes, by joining others, an irregular pattern; the follicular papules are sometimes grouped round larger flat elements, an arrangement similar to that seen sometimes in lichen planus.

THE ALOPECIAS

The alopecias may be divided into two clinical groups:

1. Diffuse alopecias affecting the whole scalp.
2. Alopecia in circumscribed patches.

Diffuse Alopecias.—These are either symptomatic, developmental, or congenital.

Symptomatic alopecia follows an acute infection such as erysipelas, typhoid fever, or influenza, and occasionally uncomplicated parturition. The hair begins to fall about six weeks after the illness, continues to fall for about the same period, and finally it regrows gradually but completely.

The alopecia that occurs sometimes in secondary syphilis has a special character; it is uneven, the scalp is riddled with clearings and irregular paths (*alopécie en clairières*). It also is temporary.

Developmental Alopecia.—The common baldness of the male requires no description. It begins most often in middle life, but often prematurely. It is gradually progressive and no recovery is possible. Heredity is the chief factor; that endocrine factors are also concerned in it is evident from the fact that it is not seen in women. Aristotle observed that children and

eunuchs never became bald, and Sabouraud said that this observation had been confirmed by a careful examination of the scalps of 350 Turkish eunuchs.

In women, particularly those with fine hair and an oily scalp, a gradually progressive loss of hair, affecting principally the vertex, is not uncommon. It is accentuated at the menopause but, unlike the masculine type, it never becomes complete. As in masculine baldness heredity is an important factor.

The rare congenital alopecias are three in number, known respectively as congenital ectodermal defect, monilethrix, and pili torti.

Circumscribed Alopecias.—These may be divided into four groups :

1. Those which follow acute infective lesions of the scalp, such as impetigo, boils, or kerion Celsi, rarely varicella ; the hair usually regrows.

2. Cicatrising alopecias. Apart from injuries and burns, permanent loss of hair with scarring may be the result of lupus erythematosus, lupus vulgaris, gumma, favus, radiodermatitis, scleroderma, lichen plano-pilaris, folliculitis decalvans, sycosis and pseudo-pelade.

3. Trichorrhexis nodosa. The condition occurs in patches, the hair of which is fuzzy and broken off short, often close to the scalp. Fracture takes place at the site of tiny swellings which can be seen with a lens, and which under the microscope are seen to resemble the partial fracture of a greenstick. Sabouraud compared the condition to that of old shaving and other brushes, and believed hair waving or dyeing, or the excessive use of shampoos, to be responsible ; but it often persists for years in spite of the strict avoidance of such causes. Rarely the hair becomes normal within a year or two.

No treatment appears to be of any value.

4. Traumatic alopecias. A patch of baldness corresponding to the part of the head in contact with the pillow is often seen in infants. The hair is rubbed away by constant rolling of the head on the pillow.

Fausse Pelades.—Patchy alopecias have been observed in epidemic form among children in institutions. They are thought to have been due to rubbing. The starting point has sometimes been the presence among the children of a case of alopecia areata.

Trichitillomania.—This is met with most often in children, and it is a symptom of restlessness like nail-biting. The child develops the habit of twisting or pulling the hair, which he pulls out or breaks off close to the scalp. The diagnosis is made by the discovery of broken hairs of different lengths.

Alopecia Areata.—The condition may consist of : (i) circumscribed patches of roughly circular outline ; (ii) large irregular patches ; (iii) complete loss of hair, sometimes involving the whole surface.

Symptoms.—The fall of hair is preceded by faint erythema of a salmon-pink colour, without subjective symptoms. As a rule the alopecia which follows is complete, but scattered hairs of normal length are occasionally seen in the patch ; these yield, however, to the slightest traction. In addition a number of short broken hairs are usually present ; these are broader and pigmented at their free extremities, while the roots are depigmented and atrophied. The presence of these hairs, which are known as " exclamation mark " hairs, indicates that the process is spreading actively.

Alopecia areata varies greatly in extent and duration. Cases in which only a few small patches are present may recover in some months. Widespread cases are more persistent, though the majority recover eventually. Those in which all the hair is lost may not recover, or partial or complete recovery is followed often by relapse from which no recovery is to be expected. Regrowth

begins in the form of downy hair, which eventually becomes replaced by fully developed hair ; this may be white at first but usually, though not always, it becomes pigmented later.

Ætiology.—Very little is known about the cause of this common condition. Heredity plays a part in a small percentage of the cases. Like vitiligo, with which it is rather rarely associated, it is believed to be the result of a functional disturbance of the sympathetic nervous supply of the skin or hair. A direct injury to the head has preceded certain cases.

The widespread belief that nervous stress or shock are common causal factors is only occasionally supported by the case histories. Alopecia areata occurs rarely in the course of Graves' disease.

There is no known rational treatment. It is customary to apply stimulating lotions or ultra-violet light in erythema doses.

SCLERODERMA AND DERMATOMYOSITIS

Scleroderma.—There are two main types :

1. Generalised, or progressive symmetrical scleroderma.
2. Circumscribed scleroderma, or morphœa.

Generalised Scleroderma.—The disease opens frequently with Raynaud's phenomenon, and this may precede other changes by weeks or months. The next phase is commonly one of œdema ; the face, hands, and forearms are first attacked, œdema is replaced by sclerosis, sometimes so superficial that it can hardly be appreciated, sometimes dense enough to impede movements of the arms, fingers, and legs ; inability to extend the fingers fully, a change spoken of as sclerodactyly, is particularly common. In the fully developed disease the sites of election are the face, the neck, and the adjoining parts of the chest and back, the fingers, hands and forearms, and the feet and legs. It may be almost universal.

The face has a peculiar and quite characteristic mask. The lips are thin and drawn over the teeth, the nose is pinched, the forehead devoid of wrinkles. Small telangiectatic tufts are present on the cheeks.

Skeletal myopathy is constant, and it is independent of overlying scleroderma ; it varies from slight myasthenia, accompanied usually by some pain, to extreme weakness and atrophy with dysphagia and nasal speech ; in such cases respiration eventually becomes impeded owing to involvement of the respiratory muscles.

Pathology.—The connective bundles of the skin lose their fibrillary structure, becoming condensed and homogeneous. In the muscles the change is that of a degenerative myopathy ; it occurs in patches and varies from loss of striation to complete disintegration.

The thyroid gland is involved in the process, the changes varying from that of a colloid goitre with increase of stroma in an early case, to atrophy and fibrosis after many years. Other endocrine glands do not appear to undergo any constant anatomical change. Calcium is sometimes deposited in the skin, and osteoporosis is found occasionally. Creatinuria is constant.

Ætiology.—The disease may occur at any age, but adults are more often attacked than children ; two congenital cases have been recorded. The

significance of the changes found in the skin, blood vessels, muscles, and thyroid gland is unknown.

Prognosis.—Severely myasthenic cases may die within a year—death is generally due to broncho-pneumonia; the majority survive for years without much change; a small number recover spontaneously.

There is no known rational treatment.

Circumscribed Scleroderma (Morphæa).—This begins with a violaceous erythematous plaque; it extends gradually, becoming ivory white in the centre and indurated. The plaque is bordered by a violaceous zone, often spoken of as the lilac ring; this marks the zone of extension of the process. There may be one or several patches of variable dimensions and shape. The process comes to an end in the course of several months or years, and is replaced by atrophy, often pigmented.

Ætiology.—Little or nothing is known of the cause of circumscribed scleroderma; it has occurred occasionally in cases of Graves' disease. Whether it is related or not to generalised scleroderma is unknown.

Treatment.—There is no satisfactory treatment.

Dermatomyositis

The early cutaneous symptoms vary in degree. There may be erythema and œdema of the face and eyelids; more often the face, neck, chest and the extremities are involved, and occasionally there is extreme œdema of universal distribution. This phase may persist with fluctuations for months, often accompanied by intermittent fever. With gradual subsidence of the œdema, the skin becomes the seat of variegated change, consisting of telangiectases, pigmentation, depigmentation, superficial roughness, and very superficial sclerosis or atrophy.

At this stage the sites of election are the face, the scalp with gradual loss of hair, the neck and the adjoining parts of the chest, back and shoulders, the backs of the fingers and hands, and the forearms and arms, especially along their extensor aspects; the legs and thighs may also be attacked, and there may also be areas of the same change of the lower part of the abdomen and back. In exceptional cases the skin changes are limited to the face and hands, and they may be quite insignificant, the case presenting then the picture of an almost pure myopathy.

Muscular Symptoms.—Weakness accompanied usually by dull pain may begin almost at once, or it may not be noticed for several weeks or months. It varies from fatigue, or inability to get up easily from a low chair, to extreme prostration with dysphagia and nasal speech. In time the muscles become wasted, abnormally firm in consistency, and retracted, so that the arms cannot be fully extended.

Prognosis.—Severe cases are sometimes fatal within a few months, others pursue a smouldering course for years, and some recover completely. Death is most often due to broncho-pneumonia.

Pathology.—In the skin superficial sclerosis is found. In the muscles the change is the same as that found in progressive scleroderma. Creatinuria is constant. Exceptionally there are deposits of calcium in the skin, and osteoporosis has also been seen.

Ætiology.—The disease is more common than is usually supposed. It occurs at all ages, though young adults are the most frequent victims. That

dermatomyositis and progressive scleroderma represent, as Langmead and others have pointed out, different aspects of a common morbid process is evident from the close similarity of the symptoms and pathology of the two conditions, as well as from the fact that every possible grade of transition between them has been seen.

Treatment.—Complete rest is necessary until definite improvement has become manifest. There is no known curative remedy. In chronic cases physical effort should be restricted to that which can be accomplished without distress. Improvement may set in even after years of weakness.

DISEASES DUE TO FILTERABLE VIRUSES

Four conditions are known to be caused by filter-passing viruses : they are Herpes Zoster, Herpes Simplex, Verruca, and Molluscum Contagiosum. Herpes Zoster has been described elsewhere (*vide* p. 632).

Herpes Simplex.—*Symptoms.*—The lesion consists usually of a single group of vesicles, but there may be two or several groups, often disposed symmetrically. The vesicles dry up in the course of four or five days, leaving a crust which separates several days later. Herpes occurs most often on the face, especially about the mouth, and on the genitalia ; but any part may be attacked, including the buccal and urethral mucous membranes. There is a marked tendency to recurrence, often at regular intervals, and in the same place.

Ætiology.—Herpes occurs at all ages from childhood onwards ; it has been transmitted from man to man with some difficulty, and from man to the rabbit with great ease. It may occur in the course of almost any fever and in coryza, but often independently of any other infection. Its cause is a filterable virus, identical with that of herpetic encephalitis in rabbits.

Treatment.—The application between attacks of two or three small doses of X-ray to the site of infection is sometimes followed by an unusually long period of freedom. The lesion itself is best treated by the application of a bland powder.

Verruca.—Warts are hard epithelial elevations ; they have a rough, horny, papilliferous surface, and they are usually of a greyish colour. They vary in dimensions and in degree of elevation. They may be flat as in the variety known as juvenile warts, raised and sessile in verruca vulgaris, filiform or pedunculated, or they may be to some extent embedded in the skin, as in the plantar and palmar types. Plantar and palmar warts are less raised than warts of similar size in other parts ; they bear some resemblance to corns, from which they can be distinguished as a rule by the presence of a slight crater-like central depression. They are nearly always painful and interfere with walking. Warts are often present on the nail-folds, extending occasionally beneath the nail to the nail-bed.

Ætiology.—A wart is essentially an epithelial hyperplasia ; the stimulus is a filterable virus. Warts are auto-inoculable and slightly infectious ; small epidemics, especially of plantar warts, are not uncommon in boarding schools.

Treatment.—For the common wart freezing with carbon dioxide snow is the most useful all-round remedy. A little acetone is added to the powdered " snow " to make a mush, and this is applied with a camel's hair paint-brush ;

each wart must be kept frozen for at least two to three minutes. Large warts generally require several treatments at intervals of about a fortnight.

Flat warts require freezing for five or ten seconds only; or they may be treated by the application of Thorium X, or trichloracetic acid, or by gentle fulguration.

Plantar warts are best treated by the single application of a large dose of X-ray, the surrounding skin being well screened with lead foil; alternatively, after curetting the wart out of its bed with a sharp spoon, the cavity is touched with the cautery or fulgurated.

Paronychial warts are difficult to treat when partly situated under the nail. This makes necessary removal of the nail, or part of it, before treating the wart by freezing or curetting.

Warts, fortunately, have a tendency to disappear spontaneously, and this happens occasionally when one or two of a considerable number have been disposed of by treatment.

Molluscum Contagiosum.—This not uncommon condition is seen most often in children. The lesions consist of epithelial tumours which vary in size from a pin's head to a pea. At first barely perceptible, they enlarge slowly to form round tumours resembling pearls. Each has a shallow central umbilication through which a creamy mass can be expressed by lateral compression.

This material is found on microscopic examination to contain large round or ovoid epithelial elements without nuclei, known as molluscum bodies, and a quantity of amorphous debris. There may be from a few lesions to hundreds, some only to be seen with a lens.

Secondary infection of the larger elements is common.

Ætiology.—Molluscum contagiosum is both contagious and auto-inoculable. It is most often seen in summer, and swimming baths are probably the chief source of infection. It is, like verruca, an epithelial tumour, and the stimulus is a filterable virus.

Treatment.—Each lesion is treated separately; the central soft portion is expressed, and a pointed match moistened with pure carbolic acid or tincture of iodine is inserted into the opening. They may also be treated by electro-coagulation.

DISEASES DUE TO FUNGI

The group of diseases caused by fungi is one of the most important in dermatology. Although many types of fungi occur in nature, only a few are parasitic on man, and these belong to a class which from their extremely simple mode of existence are known as the fungi imperfecti. These consist of round or oval spores, which are concerned with reproduction, and protoplasmic filaments known as hyphæ; a mass of hyphæ is termed mycelium.

There are three important groups of pathogenic fungi:—

1. The ringworm fungi.

2. A group of fungi resembling yeasts, of which the thrush fungus, oospora albicans, monilia Pinoyi, and the pityrosporon are examples.

3. Nocardiæ or streptothrices, of which actinomyces (*vide* p. 71) is the most important member.

The Ringworm Infections

The ringworm fungi grow on the skin and produce five types of reaction :—

1. Some attack chiefly the horny layer, with the production of scaly lesions ; also they attack the hair, which is a specialised portion of this layer.

2. The epidermis may be attacked with the production of vesicular lesions.

3. Some of the ringworm fungi excite a pustular reaction in the skin, particularly those which are pathogenic on animals, *e.g.*, cats, dogs, horses, and cattle.

4. The deeper portion of the skin may be attacked with the production of granulomatous lesions.

5. Eczematous lesions may be produced.

Ringworm Infections of the Glabrous Skin.—These may produce the following varieties of lesion :—

1. *Scaly Macular Type.*—A pink scaly macule is the initial lesion which spreads peripherally by a slightly raised and slightly erythematous edge and involutes in the centre, which remains scaly.

2. *Papular Type.*—The lesion begins and spreads in the same manner as the macular form, but there is more infiltration. Owing to the centrifugal spread, which is not quite regular, figures with polycyclic outlines are sometimes produced ; sometimes one figure is seen within another.

3. *Vesicular Type.*—The lesions begin sometimes with papules, sometimes with vesicles. They spread peripherally from the central focus, involute centrally to some extent, and leave behind furfuraceous scales and sometimes crusts of dried serum. The vesicles rest upon a reddened, often infiltrated, base.

4. *Pustular Type.*—The lesions begin as dull red papules which soon become pustules. They spread peripherally to form a solid elevated disc or plaque, round, oval, or irregular in outline, and tend to clear up partially in the centre.

5. *Granulomatous Type.*—The infection is usually derived from cattle ; the beard in man is most commonly attacked and occasionally the scalp in children. The lesions are circumscribed, indolent, tumour-like nodules or plaques involving both the subcutaneous tissue and the skin.

6. *Eczematous Type.*—Eczematoid ringworm, sometimes indistinguishable clinically from non-fungous eczema, is found most often on the feet, occasionally on the hands, in the condition best known by the American term "Athlete's foot." It may be provoked by the *Epidermophyton inguinale* as well as by several species of trichophyton, the causal fungi varying in different parts of the world.

Epidermophytosis. — The causative organism, the *Epidermophyton inguinale*, is of tropical origin. It is believed to have been introduced into England by schoolboys sent to English public schools from the East. It has become thoroughly established in the public schools, and is also to be found in swimming baths, Turkish baths, clubs, hotels, and similar institutions. The disease appears to be increasing in England. The fungus grows best in the presence of warmth and moisture and it finds these conditions especially in the inguinocrural regions, the axillæ, and the interdigital folds of the feet. There are five clinical forms of epidermophytosis.

1. *The Macular Form (Dhobie Itch)* attacks chiefly the upper inner

thigh ; both thighs are usually affected, the left more often than the right owing to the contiguity of the scrotum. The lesion spreads from the initial focus in all directions, but stops short as a rule below, at about the level of the scrotum, though in exceptional cases it may descend down the thigh as far as the knee. It may invade the perineum and the intergluteal fold, but almost always spares the inguinocrural fold. The scrotum may be attacked with the production of superficial redness or raw moist patches ; the pubes, axillæ, umbilicus, and submammary folds are often affected, but never the hair. Scattered patches, round and sometimes ringed, are occasionally widely distributed.

The lesions are irritable, red, scaly, and sharply outlined. There is less tendency to central clearing than in other forms of ringworm infection.

2. *Vesicular or Dysidrosiform.*—This and the succeeding varieties of eczematoid ringworm may also be caused by fungi of the genus trichophyton ; it may be clinically identical with the condition known as dysidrosis or cheiropompholyx ; the palms, soles, and lateral aspects of the fingers and toes are mainly affected. The fungus may be found without much difficulty by microscopical examination, in 20 to 30 per cent. solution of caustic potash, of the roof of a fresh vesicle removed from the sole or a toe. It is rarely seen in vesicles on the hands. For this reason it is evident that the hands are rarely infected directly and that the cheiropompholyx-like eruption is an allergic reaction to the focus of fungus infection on the feet.

3. *Macerated Form.*—The spaces between fingers and toes are attacked, especially the latter. The fourth interdigital cleft is always affected owing to its greater depth. The epidermis is thickened, sodden, and tough, and can be detached only with difficulty from an underlying raw surface. The periphery of the lesion presents vesicles, or the epidermis may be undermined with a ragged free edge directed towards the centre.

4. *Fissured Form.*—This form is often associated with the preceding. The natural skin folds running transversely across the under surface of the base of the toes are frequent sites. It may be complicated by occasional attacks of erysipelas of the foot or leg.

5. *Hyperkeratotic Form.*—The soles of the feet are affected, less often the palms, the horny layer being thickened and scaly ; there is a clear demarcation of the affected portion from the healthy skin.

Ringworm of the Nails.—Whatever type of ringworm infection is the cause, the nail lesions are always similar. The usual changes are thickening, with friability, vertical striation, and separation of the nail from the nail-bed.

Erythrasma.—This condition, though not related to the epidermophyton infections, is also found in the inguinocrural region and the axillæ. It consists of well-defined, clearly circumscribed reddish-yellow patches with furfuraceous scales which do not itch. The cause is the *Microsporon minutissimum.*

Pityriasis Versicolor.—Although usually included in ringworm infections this disease falls more naturally into line with the group of epidermal fungus infections caused by organisms resembling yeast, such as thrush, monilia, and pityrosporon infections. The causal organism, *Microsporon furfur*, has a predilection for covered parts. It affects chiefly the chest, abdomen, back, and shoulders, and is most commonly found in subjects with an active sweat and sebaceous secretion. The disease consists of irregular macular light brown areas, which at first sight do not always look scaly, but on gently scraping

they are easily seen to be so. The furfuraceous scales can be easily detached, and on microscopic examination in liquor potassæ the fungi are readily seen as grape-like clusters of spores disposed about short strips of mycelium.

Ringworm of the Scalp.—The scalp is commonly infected with ringworm at all ages up to puberty, but very rarely afterwards. It appears that this natural immunity may be due to a difference in the quality of the sebaceous secretion before and after puberty. According to S. Rothman the hair fat of adults contains several fatty acids with strongly fungicidal properties. The commonest cause of scalp ringworm is a small spored fungus of human origin, *Microsporon Audouini*. Occasionally the infection is derived from animals, in which case the fungus may be a small spored species, or more occasionally large spored.

Microsporon Audouini Infection of the Scalp.—The horny layer of the epidermis of the scalp is first attacked with the production of a round or irregular scaly patch. The infection then spreads downwards into the follicle encircling the hair. Just above the hair bulb the cuticle becomes frayed, and allows the mycelium to penetrate the hair. The mycelium then works upwards beneath the cuticle, and for a short distance downwards, but never reaching the bulb. From the subcuticular layer of mycelium spores are produced which penetrate the hair and coalesce to form a mosaic of spores. This extends upwards beyond the intrafollicular portion of the hair. The hair is rendered brittle, and usually breaks a few millimetres or more above the surface of the scalp. As the bulb is not infected the hair continues to grow and to break off.

Clinically *Tinea capitis*, as this condition is known, can be recognised by the presence of scaly patches with broken lustreless hairs, the normal directions of which are not followed. In addition there is often accompanying erection of the follicles. In some cases there is a moderate degree of inflammatory change in the form of superficial follicular pustulation. This is common in infections of animal origin. A special variety of pustular ringworm of the scalp, known as *Kerion Celsi*, invades the hair follicles more deeply. It gives rise to one or more raised disc-like granulomatous plaques from which the hairs, loosened by suppuration, are eventually shed spontaneously. Another special variety in which the infected hairs break off flush with the scalp, appearing in the form of tiny black dots, is known as black dot ringworm.

Microsporon infection of the scalp may be detected by Wood's light illumination. If the light from a mercury vapour lamp is passed through nickel oxide glass the luminous rays are cut off. If the scalp is viewed in a dark room under the non-luminous rays, hairs infected with microsporon fluoresce a bright green colour. In this way a single infected hair can be detected ; it is thus a valuable test of cure as well as a simple method of diagnosis. Black dot ringworm does not fluoresce.

Ringworm of the Beard (*Tinea sycosis*) may occur in two forms, a superficial variety which may be macular, papulovesicular, or pustular, or a suppurating granulomatous type resembling kerion of the scalp. The lesions of the latter type are discrete boggy swellings ; the follicles may be converted into wells of pus, or suppuration may be hardly apparent, though it is always possible to express droplets of pus from the follicles. The hairs are easily extracted with forceps, and in the course of weeks or a few months are spontaneously shed.

Trichophytides.—The suppurative varieties of ringworm infection are occasionally complicated by eruptions of generalised distribution. These appear some weeks after the onset of the infection and usually when the initial lesions are beginning to involute. The commonest variety is that known as lichen trichophyticus, usually complicating Kerion Celsi in children. This consists of small acuminate follicular papules, often capped by a filiform horny spine, occurring chiefly in groups on the trunk and limbs ; the eruption bears a close resemblance to lichen scrofulosorum. Erythema multiforme or urticaria complicating deep ringworm infection or epidermophytosis are less common forms of trichophytide.

The trichophytides are due both to the absorption of trichophytic toxin from the initial focus, to which the individual becomes sensitised, and to the dissemination in the blood stream of living fungi.

Treatment

Ringworm Infections of the Glabrous (non-hairy) Skin.—The macular, papular, vesicular, and pustular forms are easily cured by the application of tincture of iodine or Whitfield's benzoic acid ointment (*vide* Therapeutic Section). Mild mercurial ointments are also efficacious. Whitfield's ointment is particularly suitable for the macular form of epidermophytosis. The granulomatous forms are best treated by mercury perchloride fomentations of 1 : 4,000 strength.

In resistant cases a mixture containing 15 to 30 gr. of potassium iodide, or 5 to 10 minims of 10 per cent. tincture of iodine, should be given by mouth three times daily.

The interdigital variety of epidermophytosis of the feet often requires prolonged and energetic treatment. When the interdigital spaces are lined by tough, sodden epidermis it is best to remove this to begin with by means of a 12 per cent. solution of salicylic acid in spirit. This should be applied each night until all or the greater part of the horny material has been removed. A fungicide paint, such as the carbol fuchsin paint advised by A. Castellani, (*vide* Therapeutic Section) may then be applied twice daily.

For the vesicular eruption of the feet and hands Whitfield's ointment or a fungicide paint may be applied once or twice daily after bathing the feet in eusol for about ten minutes.

In cases of recent origin in which horny accumulation in the spaces is not pronounced a less concentrated solution of salicylic acid in spirit, or one containing salicylic acid and benzoic acid (*vide* Therapeutic Section), may be used in the preliminary stage of treatment. Fatty acids of the same series as those found in adult hair fat and their salts, notably propionic, undecylenic, and caprylic acids, have been employed recently with considerable success in the treatment and prevention of ringworm infection of the feet (*vide* Therapeutic Index).

Ringworm of the Nails.—Complete removal of the nail and curettage of all infected horny tissue may effect a cure. This must be followed by treatment with a strong fungicide preparation, such as 4 per cent. chrysarobin ointment, until a new healthy nail has grown. When recurrences occur in spite of the above treatment the infection can only be eradicated by operative removal of the nail matrix.

Ringworm of the Beard.—For superficial infections a fungicide ointment

is rapidly effective. The granulomatous kerion-like lesions clear up gradually with mercury perchloride fomentations of 1 : 4,000 strength.

Ringworm of the Scalp.—With the exception of Kerion Celsi, in which the hair is loosened by peripheral suppuration and spontaneously shed, and which is easily cured by local fungicide applications or by mercury perchloride fomentations, it is necessary first to epilate the hair before applying a fungicide remedy. Epilation may be accomplished (*a*) by the artificial production of follicular pustulation ; (*b*) by X-ray.

The first method of treatment may be carried out by shaving the scalp, carefully outlining the infected patches, and painting these areas daily with croton oil for twelve to fourteen days. By this means a condition resembling kerion may be produced, and in such a case the treatment will be successful, for the hair will in time be shed spontaneously. More often, however, superficial follicular pustulation results, which, while loosening the hairs somewhat, will necessitate their careful removal with forceps. This proceeding is extremely difficult and tedious.

Epilation by X-ray is the most satisfactory method of treating ringworm of the scalp. A single epilating dose is given, and the whole scalp treated. The hair falls out in nineteen to twenty-one days, and it is not difficult to cure what has now become ringworm of a non-hairy surface. Unfortunately there is a risk of some degree of permanent alopecia, though when the treatment is carried out by an expert the danger is very small.

DERMATOSES CAUSED BY ANIMAL PARASITES

Several insects and acari are able to live on the human skin and cause characteristic eruptions. The most important of these are the Pediculi (*P. capitis*, *P. pubis*, and *P. vestimentorum*), and the Acarus *Sarcoptes scabiei hominis*, responsible for scabies.

Pediculosis

There are marked differences in the size and shape of these insects by which they may be easily identified from one another. The body louse is the largest, the pubic the smallest ; the latter is broader in proportion to its length than the other two. Pediculi are provided with a pyriform head containing two jaws by which the skin is grasped, and a sucking organ. The females are more numerous than the males ; they lay large numbers of eggs provided with a chitinous envelope. These are found attached by a pedicle to the hair in the scalp and the pubic varieties, and in the clothing and on lanugo hairs in the case of the body louse. The eggs hatch out within a week, and they are mature in a fortnight. Multiplication therefore takes place at an enormous rate.

Pediculosis capitis.—The insect lives chiefly in the scalp of children but is quite commonly found in women. It appears less often in men because the ova are not easily deposited on short hairs. The lesions produced by the presence of *P. capitis* vary within wide limits according to the susceptibility of the individual. Some persons are able to harbour enormous numbers of the insect without symptoms, but in others the irritation set up by the bites produces eruptions of varying severity, with more or less severe pyogenic

infection. Pyodermatitis may be in the form of impetigo or a pustular folliculitis, and it may be accompanied by abscesses of the scalp. In severe cases the hair may be matted together by crusts of dried serum which overlie a scalp bathed in pus (*Plica polonica*). In such cases, as well as in milder ones, the pyodermatitis extends sometimes to the post-auricular grooves, the neck, shoulders, and upper part of the back. Linear scratch marks, excoriations, and pyodermatitis may be present in these regions also without lesions in the scalp, owing to the fact that the pediculi are able to leave the scalp for feeding purposes though not for propagation. Serious sequelæ of *Pediculosis capitis* are often met with in the form of impetiginous dermatitis and chronic folliculitis of the scalp, blepharitis, and post-auricular impetiginous eczema. The glands in the neck may be secondarily enlarged.

Pediculosis corporis.—The body louse is larger than the head louse, and lives on the non-hairy parts of the skin, while the ova are deposited chiefly in the seams of the clothes but are found also attached to lanugo hairs. The type and degree of the eruption varies with the susceptibility of the individual. Infestation with body lice is almost invariably associated with conditions that necessitate sleeping in day clothes; hence it is met with chiefly in the destitute, particularly the aged, and in soldiers on active service. The lesions are found in places where the clothes are in close contact with the skin, such as the shoulders, scapular regions, the posterior axillary folds, the abdomen, and the anterior aspects of the thighs. The forearms and hands, legs and feet are rarely attacked. The bite of the insect causes an urticarial wheal of more or less intensity. Linear excoriations caused by scratching are also present. Pigmented patches are found in prolonged cases, and in the most severe forms the skin may become thickened from incessant scratching and almost uniformly pigmented. Sometimes pigment may be found in the buccal mucous membrane. A certain degree of debility accompanies *Pediculosis corporis* in some cases, and is attributed to a toxin introduced by the insect. The pigmentation is believed to be of like origin. *Pediculi corporis* are responsible for the transmission of typhus.

Pediculosis pubis.—*P. pubis*, or the crab louse, lives on the pubic region, but invades the neighbouring portion of the thighs and abdomen as well. The axillary hairs, eyebrows, and eyelashes are occasionally invaded, particularly in aged subjects. Infection is generally though not always acquired through sexual intercourse. The insect is provided with claws by which it is able to grasp a hair. It feeds by plunging its head into the mouth of the follicle bearing the hair to which it is attacked. The ova are found attached to the hairs close to their bases. The bites give rise to more or less severe itching, and often a follicular pustular eruption on the pubes, inner aspects of the thighs, and lower portion of the abdomen. In addition, pigmented patches of a peculiar slate-blue colour are sometimes found on the abdomen or thighs. These are pathognomonic of the disease.

Treatment.—*Pediculosis capitis.*—A close haircut is naturally the simplest way of curing the condition. It is necessary in cases complicated by severe pyogenic infection; for female children and women, however, this drastic remedy is undesirable. As the result of trials on a large scale during the late war an oily preparation known as lethane oil has been found to be extremely efficient for the treatment of head lice (see Therapeutic Index). After a preliminary shampoo with soft soap and borax (borax, 1 oz.; soft soap, ½ lb.; hot water, 1 quart), followed by drying, the oil is applied out of

a dropper in the scalp along partings, four on each side of the head ; it is then gently massaged over the scalp with the tips of the fingers to ensure even distribution. The hair should not be washed for a week. The single application is said to kill all lice and nits ; the latter may be combed out if desired after a shampoo at the end of treatment with a fine metal comb.

Pediculosis corporis.—During the first world war infestation of troops in the front line was the rule rather than the exception. In the late war the underclothes of all land forces were impregnated with the chemical substance known as D.D.T.—dichloro-diphenyl-trichlorethane. The success of this prophylactic measure may be judged by the fact that pediculosis of the body was almost completely absent in the British Army. For the treatment of *Pediculosis corporis* a powder containing 5 per cent. of the insecticide is used.

Pediculosis pubis.—Lethane oil, benzyl benzoate cream, and D.D.T. powder are effective remedies.

Scabies

This common parasitic disease is caused by an acarus, *Sarcoptes scabiei hominis.* The female penetrates the epidermis and burrows immediately beneath the horny layer, depositing ova in her progress. The presence of the parasite gives rise to a vesicle of about the size of a pin's head or larger, immediately in front of which the acarus can sometimes be seen as a tiny brownish spot. Runs are found in the following sites of predilection : the wrists, particularly the ulnar margin, the sides of the fingers—these are by far the most common sites ; then follow the posterior surface of the elbows, the feet, the penis and scrotum, the fold of the nates, and the axillæ. In children burrows are also found on the palms and soles. The ova hatch out in sixty to one hundred hours or longer ; the larval parasite makes its own burrow, which is said to be marked by a vesicle ; succeeding stages, nymph and adult male, nymph and immature female, also burrow and probably wander as well, but the mature female having made her burrow (the run) does not move from it.

Maturity is reached in eight days or longer from the laying of the egg. At 13° C. mites may survive for as long as fourteen days away from their host, but not longer than forty-eight hours at higher or lower temperatures. The lesions of uncomplicated scabies are of three types : (i) runs consisting of dirty greyish lines, straight or sinuous, and usually less than $\frac{1}{2}$ cm. long, terminated by a vesicle ; (ii) vesicles ; (iii) papular lesions. The last two are found on the hands, fingers, and wrists, the feet, the legs and forearms, the sides of the chest, the abdomen, the inner aspects of the thighs and the genitals, and in the natal clefts. They occur in greatest numbers in the immediate neighbourhood of the breeding grounds, becoming more sparse in the intervening areas. A group of papules on the point of one or both elbows is almost always present in well-developed cases. The presence of one or several indolent papules or small nodules on the penis and scrotum is also a highly characteristic feature of scabies. The face and scalp are always spared and the neck is hardly affected. The back also is attacked to a minor degree or not at all.

The distribution of the lesions contrasts with that of *Pediculosis corporis.* Itching is first experienced usually from four to six weeks after the parasite has gained a foothold ; from then onwards it becomes increasingly severe. Accessory lesions in the form of linear excoriations, pyodermia, and traumatic

eczema are common. Scabies is the most frequent cause of eczema of the nipple in women. Unfortunately both complications may be very troublesome. In babies and young children scabetic lesions on the wrists, hands, and fingers are generally far more numerous than in adults, and a severe pyodermia of the hands is not uncommon. This infection and the eczematisation which may accompany it add considerably to difficulties in treatment. In adults also, particularly those with fair sensitive skins, infection and eczema may mask the underlying scabies.

According to L. Mellanby, scabies is probably transmitted almost entirely by skin contact. He tried to infest volunteers through clothes and bedding. With bedding he failed altogether; and of thirty-two who wore clothes immediately after they had been worn by scabetic patients, only two subsequently developed scabies; with longer intervals no infestation took place. Three out of four volunteers who slept with scabetic patients became infested, the earliest lesions appearing from eight to twelve days later. He found that no complaint of itching may be made for six or seven weeks.

Treatment consists of the thorough application of one of several remedies (*vide* p. 843), of which benzyl benzoate appears to be accepted at present as probably the most efficient. A bath is taken, the patient covered with soft soap and scrubbed; immediately after the bath, a mixture of benzyl benzoate, soft soap and spirit in equal parts is brushed on all over from the neck downwards. This gives rise to stinging, which, however, passes off in about half an hour. Two or three such treatments are generally enough, or a cream containing 25 per cent. of benzyl benzoate may be rubbed in by hand (see Therapeutic Index). When an ointment is used the treatment is a little more prolonged. After the preliminary hot bath and scrubbing, the ointment is rubbed in thoroughly from the neck downwards and reapplied twice daily for the following three or four days; a final bath is taken at the end of this period and a complete change of clothing made. At the end of treatment clothes and bedclothes should be changed; clothes that cannot be laundered should be disinfected by heat. Any temperature above 49° C. will kill the sarcoptes in five minutes.

All these treatments cause some irritation, and dermatitis is a common sequel; after treatment with sulphur ointments the skin, especially in fair-skinned subjects and in children, may become red and scaly; in some cases the patient assumes that he is not cured, and adds to the trouble by further treatment. Dermatitis also occasionally follows treatment with benzyl benzoate, owing to allergic sensitivity; in such cases the dermatitis is severe though fortunately short-lived.

Eczema complicating scabies requires special treatment after the parasitic infection has been dealt with; White's crude tar paste diluted with one or two parts of zinc ointment is useful in these cases (*vide* Therapeutic Section, p. 844).

EXTERNAL TREATMENT

Cutaneous lesions often require treatment by surgery, the galvanocautery, electro-coagulation, electrolysis, carbon dioxide snow, X-ray, and radium. For information concerning such methods the reader is referred to works on dermatology.

In addition local applications of various kinds are of great importance

in the treatment of disease of the skin. Sometimes the restoration of superficial damage is best achieved by attention to cleanliness and the application of protective lotions, liniments, creams, or pastes. In other cases it is desirable to use chemical agents having bacteriostatic, antiseptic, fungicidal, or antiparasitic properties, or rubefacients, reducing and caustic agents. Some of these may be incorporated into powders, lotions, creams, pastes, ointments, and paints, while occasionally they are used in the pure state.

It is not necessary to employ a large number of remedies.

Cleansing Agents.—It is useless to apply a remedy to a lesion which is covered with a crust or scab until the latter has been removed. Water, being hypotonic, exerts a macerating action on damaged tissues and is generally unsuitable for this purpose ; *normal* saline may, however, be used. Simple lotions, to which small quantities of antiseptics may be added if necessary, often serve the double purpose of cleansing and protecting a damaged skin. The starch and boric poultice is a valuable cleansing agent. To four tablespoonfuls of starch are added one or two teaspoonfuls of boric acid and enough cold water to make a thick paste. Boiling water is added slowly with continuous stirring until the starch bursts. The poultice is spread out thickly on linen or lint, and the surface to be placed against the skin covered with butter muslin.

Protective and Soothing Remedies.—An acutely inflamed surface requires an application with cooling and soothing properties such as a simple lotion, liniment, or powder. Lotions and oily liniments by facilitating drainage are suitable applications for weeping surfaces. Serous oozing or weeping is generally succeeded by desquamation, which is usually the result of parakeratosis. The superficial cells have not undergone their normal transformation into the homogeneous horny layer and are lacking mainly in fat. Creams, pastes, and ointments are used to supplement this deficiency until the normal horny layer has been reformed. To these, other substances with anti-pruritic or mildly stimulating properties may sometimes be added.

	Indications.
Calamine Lotion— Prepared calamine, 15 grains. Zinc oxide, 15 grains. Glycerin, 20 minims. Lime water to 1 fluid ounce. Solution of coal tar, 0·5 to 1 fluid drachm, or phenol, 5 to 10 grains, may be added to each fluid ounce to allay pruritus.	May be used for erythema, urticaria, the erythematous and early vesicular stage of eczema, and eczematous dermatitis.
Watery Paste— Zinc oxide, 24 per cent. Titanium oxide, 21 per cent. Colloidal kaolin, 8·5 per cent. Glycerin, 15·5 per cent. Water, 31 per cent.	(Semon, H. C., and Hermann, F.) Siccolam, B.D.H. Acute weeping or erythematous dermatitis.
Lead Lotion— Diluted solution of lead subacetate B.P.	Indications as above.
Calamine Liniment— Zinc oxide. Calamine, of each 480 grains. Powdered gum tragacanth, 60 grains. Phenol, 10 grains. Glycerin, 10 minims. Olive oil, 4 fluid ounces. Water to 20 fluid ounces.	Suitable for the vesicular and weeping stage of eczema.

Protective and Soothing Remedies—*continued.*

Creams.—Creams are fatty preparations containing water.

Zinc Cream, B.P.C.— *Indications.*
Zinc oxide, 1 ounce.
Anhydrous lanolin, 2 drachms.
Olive oil, 1 fluid ounce.
Lime water, 6 fluid drachms.
Desquamative stage of eczema.

Water-soluble base—
Liquid paraffin, 14 per cent.
Soft white paraffin, 10·5 per cent.
Cetyl stearyl alcohol, 10·5 per cent.
Water to 100 per cent.
(Medicaments may be added.)

In recent years the introduction of a large series of emulsifying agents of a new type has opened up new possibilities in external treatment. The emulsifier chiefly used in this country is Lanette wax SX ; it is a mixture of 90 per cent. cetyl alcohol and stearyl alcohols containing 10 per cent. of a sodium alkyl sulphate. When this or an emulsifier of a similar type is added to various oils, *e.g.*, liquid paraffin or soft paraffin, which do not mix with water, the mixture readily forms an emulsion with water, known as an oil in water emulsion. Into such an emulsion or cream various medicaments may be introduced. A great advantage of such a vehicle is that by decreasing surface tension between the preparation and the skin, it permits far more intimate contact of the dissolved medicament with the skin than is possible when the older type of base is used. It has the additional advantage of being readily removed with water. The new type of vehicle is usually termed a " water-soluble base."

Pastes.—These are preparations having usually a fatty or petroleum base in which *inert powders such as starch, kaolin, or zinc oxide are incorporated.*

Compound zinc paste (Syn. Lassar's Paste) B.P.C. *Indications.*
Salicylic acid, 2·0.
Zinc oxide, 24·0.
Starch powder, 24·0.
Soft paraffin, 50·0.
A protective paste suitable for eczema in the desquamative stage.

Ointments—
Soft paraffin, 150 grains.
Glycerin of starch, 150 grains.
Lanolin to 1 ounce.
Emollient ointment suitable for ichthyosis.

Powders—
Boracic acid powder, 10·0.
Starch powder, 10·0.
Oil of geranium, 0·2.
Purified talc to 100·0.
(Mix and sift.)
Local application for herpes catarrhalis, herpes zoster, intertriginous dermatitis. Napkin erythema, intertriginous erythema, erythematous stage of eczema.

Antiseptics.

Lotions—
Alibour water (Guy's Hospital formula).
Copper sulphate, 2·0.
Zinc sulphate, 7·0
Saturated aqueous solution of camphor, 300·0.
(Dissolve and mix.)
For removal of crusts and for cleansing the surface of impetigo contagiosa, Bockhardt's impetigo, and pyodermatitis in general. Must be diluted with 5 to 10 parts of water.

Mercuric chloride, 0·1 grain.
Sodium chloride, 5 grains.
Water to 1 fluid ounce.
(Dissolve and mix.)
As above.

Antiseptics—*continued.*

Lotions—continued.	*Indications.*
Sodium sulphacetamide, 2·5 to 10 per cent. Distilled water to 100 per cent. Penicillin, 500 to 1,000 units to 1 cubic centimetre.	As above.
Paints—	
Silver nitrate, 5 to 20 grains. Spirit of nitrous ether, 1 fluid ounce. (Dissolve.)	For painting on fissures caused by streptococci.
Gentian violet, 0·5 to 1 per cent. Calamine lotion to 100 per cent.	As above.
Pastes—	
Precipitated sulphur, 30 to 45 grains. Zinc oxide, 60 grains. Kaolin B.P., 15 grains. Benzoated lard to 1 ounce.	Bockhardt's impetigo, figurate type of seborrhœic dermatitis, pustular acne.
Ointments—	
Ammoniated mercury, 5 to 20 grains. Soft paraffin to 1 ounce.	Impetigo contagiosa, pyodermatitis.
Yellow mercuric oxide, 5 to 10 grains. Soft paraffin to 1 ounce.	As above.
Sulphathiazole, 5 to 10 per cent. Water soluble base to 100 per cent.	As above.

Fungicide Preparations.

Paints—	
Chrysarobin, 60 grains. Acetone, 3 fluid drachms. Rectified spirit to 1 fluid ounce.	Ringworm, especially epidermophytosis of interdigital folds.
Benzoic acid, 25 grains. Salicylic acid, 15 grains. Acetone, 2 fluid drachms. Rectified spirit to 1 fluid ounce. (Dissolve and mix.)	As above.
Carbol-fuchsin Paint (Castellani)—	
Sat. sol. of basic fuchsin, 10 c.c. 5 per cent. aqueous sol. of phenol, 100 c.c. Filter and add Boric acid, 1 gramme. Allow to stand for two hours and add Acetone, 5 c.c. Allow to stand for two hours and add Resorcin, 10 grammes. (Keep in a dark-coloured and well-stoppered bottle.)	Epidermophytosis.
Ointments (Whitfield's ointment)—	
Benzoic acid, 25 grains. Salicylic acid, 15 grains. Soft paraffin, 120 grains. Coco-nut oil to 1 ounce.	Ringworm of non-hairy surface, also of the scalp after epilation.
Zinc undecylenate, 20 per cent. Undecylenic acid, 5 per cent. Liquid paraffin, 50 per cent. Lanette wax SX., 10 per cent. Water, 15 per cent.	As above.

Anti-parasitic Remedies.

	Indications.
Benzyl benzoate, 25 per cent. Lanette wax SX, 2 per cent. Water to 100 per cent.	Scabies.
Lethane oil.	Pediculosis capitis and pubis.

Keratolytic drugs, having the property of softening and destroying keratin and so producing maceration or exfoliation of horny tissue, may be incorporated into pastes, ointments, and other preparations. The most important is salicylic acid.

Keratolytic Paste—	*Indications.*
Resorcin, 10·0. Camphor, 10·0. Soft soap, 15·0. Precipitated sulphur, 30·0. Prepared chalk, 5·0. Soft paraffin, 30·0.	Acne vulgaris, particularly of the back and shoulders: should be applied for four or five days only, then followed by a milder sulphur paste or lotion for a week before repetition.
Lotion—	
Sulphurated potash, 2·0. Rose water, 8·0. (Dissolve solution No. 1.) Zinc sulphate, 2·0. Rose water, 8·0. (Dissolve solution No. 2; mix equal parts of Nos. 1 and 2 for use.)	Acne vulgaris: produces exfoliation. Solution No. 1 must be made freshly once in three weeks.
Sulphurated potash. Zinc sulphate of each, 1 per cent. Glycerin, 15 per cent. Lanette wax SX, 5 per cent. Carbowax 4000, 20 per cent. Water, 58 per cent.	Acne.
Ointment—	
Salicylic acid, 5 to 25 grains. Soft paraffin to 1 ounce.	Palmar and plantar keratoses, corns, psoriasis, and any condition in which a preliminary removal of accumulated horny material is necessary.

Reducing Agents.—A number of chemical substances commonly used in dermatology have been designated reducing agents. Some of them, *e.g.*, pyrogallic acid, chrysarobin, and lenigallol, are reducing agents in the chemical sense, but others such as tar, ichthyol, and sulphur, while having a similar therapeutic action, are not known to have an avidity for oxygen. Tar and ichthyol have anti-pruritic properties.

Ointments—	*Indications.*
Chrysarobin, 20 to 60 grains. Soft paraffin to 1 ounce. (Mix.)	Psoriasis.
Dithranol B.P., 0·25 to 2 per cent. Soft paraffin to 100 per cent.	Psoriasis.
Pyrogallic acid, 7 per cent. Chrysarobin, 10 per cent. Liq. picis carbonis, 20 per cent. Sulphur, 10 per cent. Vaseline to 100 per cent. (Meirowski.)	Psoriasis.
Solution of coal tar, 30 to 60 minims. Ammoniated mercury, 10 grains. Salicylic acid, 10 grains. Paraffin ointment B.P. to 1 ounce.	Psoriasis.

Reducing Agents—*continued.*

Ointments—continued.	*Indications.*
Oil of cade, 30 grains. Sulphur, 10 grains. Salicylic acid, 10 grains. Soft paraffin, 120 grains. Coco-nut oil to 1 ounce.	Psoriasis of the scalp. Chronic seborrhœic dermatitis of the scalp, pityriasis capitis.
Pastes—	
Solution of coal tar, 40 to 60 minims, or ammonium ichthosulphonate, 5 to 10 grains. Zinc oxide. Starch in powder, of each 90 grains. Soft paraffin to 1 ounce.	Lichenified and scaly eczema. Seborrhœic dermatitis of the pityriasiform, and the acute and subacute follicular papular types.
Crude coal tar, 2·0. Zinc oxide, 2·0. Starch in powder, 16·0. Soft paraffin, 16·0.	As above. Especially useful for lichenified eczema and for infantile eczema.

The tar and zinc oxide should be triturated thoroughly, also the starch and paraffin, then the two parts incorporated; resultant paste should be almost black. It may be diluted with one or two parts of zinc ointment.

Caustics.—The use of caustics for the destruction of warts and other cutaneous tumours is unsatisfactory, and has become largely superseded by carbon dioxide snow, the galvano-cautery, electro-coagulation, X-ray, and radium. Certain caustics are, however, of value in the treatment of lupus, and their present extensive use is likely to continue. Trichloracetic acid may sometimes be applied successfully to the treatment of warts.

	Indications.
Acid solution of mercuric nitrate.	Exerts a selective caustic action on lupus tissue. It is painted on the lesions about once in three weeks.
Picric Brass Paste— Basic copper sulphate, 85 per cent. Zinc sulphate, 14 per cent. Picric acid 1 per cent.	Applied to patches of lupus under strapping, changing every 24 to 48 hours until caustic has eaten into the nodules.
Zinc chloride.	Used as a solid stick for application to lupus of mucous surfaces.
100 per cent. solution of trichloracetic acid.	Warts, particularly genital or seborrhœic warts.

Rubefacients.

Paints—	
Tincture of capsicum. Ammoniated camphor liniment B.P., of each equal parts.	Unbroken chilblains.
Ointment—	
Resorcin ointment, 24 grains. Carbolic acid ointment, 240 grains. Zinc oxide, 120 grains. Soft paraffin, 2 ounces.	Broken chilblains.

GEOFFREY B. DOWLING.

APPENDIX I

EXAMINATION FOR LIFE ASSURANCE

IT may be permissible to remind the physician who is unaccustomed to life assurance work that during an examination for life assurance he is for the time being the servant of a company and not the adviser of a patient. Consequently he should endeavour to give an entirely unbiased opinion on the life, remembering that he is not the " family doctor " putting the best possible aspect on the case in his patient's interest, and that no hint as to the result of his examination must be given to the examinee. Also, it should be borne in mind that in every examination of this nature the examiner's duty is to advise the company whether the applicant's prospects of longevity are " average," " under average," or definitely " bad," an entirely different proposition from that which usually confronts a physician.

The medical referee chosen to conduct a life assurance examination is generally some doctor other than the proposer's medical attendant. The main reason for this practice is that it is obviously unfair to place the proposer's own doctor in the invidious position of deciding between his duty to the office and his natural inclination in favour of his patient. Moreover, the company or its chief medical adviser may require further information on some doubtful point arising out of the examiner's report, and the private medical attendant's views, unprejudiced by any previously expressed opinion, will probably be more helpful in this respect than those of any other doctor.

The medical report form is divided into two parts ; the first concerns the proposer's family and personal history, including questions as to the general mode of living. The second part records the results of physical examination of the applicant, and concludes with a summary for classifying the life.

Precise information should be obtained from the proposer as to the causes of death of any members of his family, and as to the duration of their last illnesses. In attempts to discover tendencies to disease, a study of the family history is most important. This is especially true in cases where a parent has died of phthisis, as statistics show clearly that among the children of tuberculous parents there is an increased incidence of the disease as compared with that among the population as a whole. Moreover, the risks of developing phthisis are greater during early adult life than after the age of thirty-five or forty, and therefore a family history of phthisis is more serious if the proposer is young. If he is under weight or apparently in any way unfit, it is wise in the presence of a family history of phthisis to recommend the office to decline or, at any rate, to defer the proposal. In any case no proposer under thirty-five, however fit, should be recommended at ordinary rates if a parent has died of consumption.

After the family history has been dealt with the applicant is asked

whether he has suffered from a number of specified diseases. If the proposer has had any of these diseases, brief particulars of the illness, with a note of its duration and severity, should be inserted. If, for instance, an affirmative answer is given to the question regarding consumption, blood-spitting, or pleurisy, the date of the attack should be mentioned, whether tubercle bacilli were found in the sputum, and whether any X-ray photographs of the chest are available. With a history of pleurisy, inquiry should be made as to whether an effusion was present. If so, acceptance should not be recommended until at least five years have elapsed. Again, if syphilis is admitted, the date of the primary infection, the duration of the treatment, and the date of the last Wassermann test should be stated. With regard to any past history of discharge from the ear, it is important to know when the discharge last occurred.

Full details should be given regarding any major illness, including the length of stay in bed and the total time away from work.

Following this section of the report, questions are asked regarding habits in the use of alcohol and drugs. In the answers to these questions the examiner should recognise that there will be a tendency to understate the amount of alcohol consumed. He should also bear in mind the proposer's occupation and circumstances.

This concludes the interrogation of the proposer. While recording the answers to the questions the examiner will have ample opportunity of forming an opinion not only on the sincerity of the applicant but also on his general appearance, development, and usual mode of living. Indeed, by this time he will probably have formed a shrewd idea of the proposer's chances of being accepted.

The physical examination is now begun, and its various sections will be dealt with in the order in which they commonly appear in report forms.

1. *Measurements.*—A table of average heights and weights (in ordinary clothes) is appended (*vide* p. 848). Offices usually allow considerable deviation from the "average" where the examination is otherwise favourable. Some companies fix a definite percentage above or below the average as the limit within which lives can be accepted at the ordinary rates. This method, however, can hardly be regarded as a satisfactory way of dealing with any abnormality. A far better standard for judging "over weights" should be the distribution of fat, remembering that heavy persons are not as a rule good risks, particularly where there is a tendency to obesity. On the other hand, "light weight" by itself should not be considered an unfavourable feature, provided that it has been constant, that the chest expansion is good, and the family and personal histories unexceptionable. In all cases a chest expansion of 2 in. should be regarded as the minimum. It may be necessary, in some instances, to measure the expansion more than once, owing to the proposer's faulty method of breathing. An abdominal measurement exceeding the girth of the unexpanded chest is always an unsatisfactory feature, and such proposers can rarely be accepted at ordinary rates.

2. *Cardio-vascular System.*—Note briefly, but exactly, any abnormality of the heart. If a murmur is present a note should be made as to its timing and character. In the case of systolic murmurs, it is particularly important to state whether they vary with phases of respiration or with posture. Systolic murmurs which are functional in character are no bar to acceptance

at ordinary rates. A systolic murmur in persons of middle age and over should be viewed with grave suspicion.

A blood-pressure estimation should be done in all examinations. The first attempt may give an unduly high reading, often due to nervousness or excitement, and subsequent readings may be quite normal. A systolic pressure persistently over 150, especially in proposers between forty and fifty years of age, may indicate the onset of hyperpiesia, and such cases should rarely be recommended for acceptance even with an increased premium. Low pressures, provided they are not below 100 and the proposer is unexceptionable in other respects, are not of real significance. Diastolic pressures over 100 always indicate pathological hypertension. It must, however, be realised that in some cases it is difficult, if not impossible, to estimate the diastolic pressure with accuracy.

The pulse-rate, when first taken, is often unduly rapid owing to nervousness, but a later reading may show it to be within normal limits. When tachycardia is thought to be of nervous origin the pulse-rate should be taken again after the proposer has rested for a few minutes. Extrasystoles in a young man are often without pathological significance, but when they occur over the age of forty they must be viewed with suspicion.

3. *Respiration.*—Absence of abnormal physical signs is no indication that the lungs are healthy, and in all cases of doubt an X-ray of the chest should be recommended.

4. *Digestion.*—Should a proposer admit to attacks of dyspepsia, careful inquiries should be made into the details of symptoms and treatment. A private medical attendant's report should be recommended. Peptic ulcer, whether treated by medical or surgical methods, is rarely, if ever, acceptable at ordinary rates of premium, and such cases should be deferred until at least two years have elapsed without symptoms, whether operation has been performed or not.

5. *Genito-urinary System.*—The urine is examined for albumin and sugar. Albuminuria is frequently found at life assurance examinations in persons under twenty-five years of age. The practice of most offices is to require three further specimens at later dates ; at least one of these should be examined microscopically. Provided all the subsequent specimens are free of albumin, the life may be recommended at ordinary rates. The discovery of sugar in a young proposer may be of little significance, but such a case always demands a most thorough investigation, including a glucose tolerance curve. Albuminuria or glycosuria in older people is a more serious matter and such cases must usually be declined.

Conclusion.—A definite opinion should always be expressed as to whether the life is an average risk, acceptable at ordinary rates, or an under-average risk, which might be taken with a loading, or whether the proposal should be deferred or declined. Where the life is not an average one, a brief statement should be made of the grounds on which such a decision has been reached.

J. J. Conybeare.

HEIGHTS AND WEIGHTS

Male Lives

A Table deduced from the records of seven Life Offices in respect of 28,697 Medical Examinations for Assurance made during the years 1921 and 1922 (weight clothed).

(By permission of the Institute of Actuaries)

Age next Birthday.	HEIGHT.																					
	5′ 4″		5′ 5″		5′ 6″		5′ 7″		5′ 8″		5′ 9″		5′ 10″		5′ 11″		6′ 0″	
	st.	lbs.	st.	lbs.	st.	lbs.	st.	lbs.	st.	lbs.	st.	lbs.	st.	lbs.	st.	lbs.	st.	lbs.
20	8	12	9	1	9	5	9	8	9	12	10	2	10	5	10	9	10	13
21	8	13	9	3	9	6	9	9	9	13	10	3	10	6	10	11	11	1
22	9	0	9	4	9	7	9	11	10	0	10	4	10	8	10	12	11	2
23	9	1	9	5	9	8	9	12	10	1	10	5	10	9	10	13	11	3
24	9	2	9	6	9	9	9	13	10	2	10	6	10	10	11	0	11	4
25	9	3	9	7	9	10	10	0	10	3	10	7	10	11	11	1	11	5
26	9	4	9	8	9	11	10	1	10	4	10	8	10	12	11	2	11	6
27	9	5	9	9	9	12	10	1	10	5	10	9	10	12	11	3	11	7
28	9	6	9	10	9	13	10	2	10	6	10	9	10	13	11	4	11	8
29	9	7	9	11	10	0	10	3	10	7	10	10	11	0	11	5	11	9
30	9	8	9	11	10	1	10	4	10	8	10	11	11	1	11	5	11	10
31	9	9	9	12	10	1	10	5	10	9	10	12	11	2	11	6	11	11
32	9	9	9	13	10	2	10	5	10	10	10	13	11	2	11	7	11	12
33	9	10	9	13	10	3	10	6	10	10	10	13	11	3	11	8	11	12
34	9	10	10	0	10	3	10	7	10	11	11	0	11	4	11	9	11	13
35	9	11	10	1	10	4	10	8	10	12	11	1	11	4	11	9	12	0
36	9	11	10	1	10	4	10	8	10	12	11	2	11	5	11	10	12	1
37	9	12	10	2	10	5	10	9	10	13	11	2	11	6	11	11	12	2
38	9	12	10	2	10	6	10	10	11	0	11	3	11	7	11	12	12	3
39	9	13	10	3	10	6	10	10	11	0	11	4	11	8	11	13	12	3
40	9	13	10	3	10	7	10	11	11	1	11	5	11	9	12	0	12	4
41	10	0	10	4	10	7	10	11	11	2	11	5	11	9	12	0	12	5
42	10	0	10	4	10	8	10	12	11	2	11	6	11	10	12	1	12	6
43	10	1	10	4	10	8	10	12	11	3	11	6	11	11	12	2	12	6
44	10	1	10	5	10	9	10	13	11	3	11	7	11	12	12	2	12	7
45	10	2	10	5	10	9	10	13	11	3	11	8	11	12	12	3	12	8
46	10	2	10	6	10	10	11	0	11	4	11	8	11	12	12	3	12	8
47	10	2	10	6	10	10	11	0	11	4	11	9	11	13	12	4	12	9
48	10	3	10	6	10	10	11	1	11	5	11	9	12	0	12	5	12	10
49	10	3	10	7	10	11	11	1	11	5	11	10	12	0	12	5	12	10
50	10	3	10	7	10	11	11	1	11	6	11	10	12	1	12	6	12	11
51	10	4	10	8	10	11	11	2	11	6	11	11	12	1	12	6	12	11
52	10	4	10	8	10	12	11	2	11	6	11	11	12	2	12	6	12	11
53	10	4	10	9	10	12	11	2	11	7	11	11	12	2	12	7	12	12
54	10	4	10	9	10	12	11	3	11	7	11	12	12	3	12	7	12	12
55	10	4	10	9	10	12	11	3	11	7	11	12	12	3	12	7	12	12
56	10	5	10	9	10	13	11	3	11	8	11	12	12	3	12	8	12	13
57	10	5	10	9	10	13	11	3	11	8	11	12	12	3	12	8	12	13
58	10	5	10	9	10	13	11	3	11	8	11	13	12	3	12	8	12	13
59	10	5	10	9	10	13	11	3	11	8	11	13	12	4	12	8	12	13
60	10	5	10	9	10	13	11	3	11	8	11	13	12	4	12	8	12	13

APPENDIX II

AVIATION MEDICINE

AVIATION Medicine is the study of the problems which occur when the body is subjected to the new environment of flight. Its aim is to observe how man becomes adapted to the altered circumstances, and to increase efficiency by bridging the gap between human and aircraft performance so that the maximum use can be made of the machine. The fundamental problems considered here are those caused by decreased atmospheric pressure and by changes in acceleration. The subsidiary topics, such as exposure to changes of temperature, noise, vibration, and the effects of toxic gases, are essentially the same in the air as on the ground, although their consequences are more serious in flight, and protection against their effects presents special difficulties. Information on these problems can be obtained in textbooks of aviation medicine.

THE EFFECTS OF DECREASED ATMOSPHERIC PRESSURE

Decreased atmospheric pressure causes oxygen lack, expansion of gas in the ears, sinuses, and gut, and decompression sickness. A brief outline of the causation and symptoms of these effects is given and the question of their prevention is discussed.

I. Oxygen Lack

(1) **Cause.**—Air consists of approximately 21 per cent. oxygen and 79 per cent. nitrogen, and this composition is virtually constant up to heights of about 70,000 ft. Oxygen lack, or anoxia, is due to the fact that the partial pressures exerted by oxygen and nitrogen in air vary with altitude, although the percentage composition remains the same. Air has weight, and at ground level it maintains a pressure on the body of 14·7 lbs. per square inch, or one atmosphere. At 18,000 ft. this pressure is halved (7·35 lbs. per square inch), and at 34,000 ft. it is reduced to a quarter (3·72 lbs. per square inch). It is the weight or pressure of oxygen in the lungs which forces it through the capillary endothelium of the alveoli, where it is taken up by the hæmoglobin of the circulating red corpuscles. With increasing altitude the oxygen tension in the blood falls, and at heights above 10,000 ft. the decrease in blood saturation begins to affect efficiency.

(2) **Prevention.**—Oxygen lack at altitude is prevented by increasing the partial pressure of oxygen in the lungs at the expense of the nitrogen. This is done by supplying additional oxygen through a face mask. The total pressure of oxygen in the alveoli is then sufficient to maintain full saturation of the blood. This is satisfactory up to an altitude of 36,000 ft.,

but above this height the total atmospheric pressure is so small that even when pure oxygen is breathed blood saturation falls and oxygen lack occurs. Above this height either a pressure suit or a pressure cabin must be used if the blood is to remain fully saturated. An altitude of 44,000 ft. is the limit at which flight is possible with a reasonable degree of safety if a pressure device is not employed. A man breathing pure oxygen at this height without a pressure cabin suffers from approximately the same degree of oxygen lack as a man breathing air at 19,000 ft.

(3) **Effects.**—(*a*) *Brain.*—In aviation there is no doubt that the most important effect of oxygen lack is its action on the cerebral cortex, where it is responsible for loss of judgment without insight or realisation. The effect of anoxia on the cortex closely resembles that of alcohol. Simple errors of calculation and manipulation will pass undetected, and euphoria, irresponsibility, and signs of aggression may develop. Lethargy, sleepiness, stupor, and unconsciousness follow each other without the subject realising that anything abnormal has taken place. Even minor degrees of anoxia may give rise to loss of memory for events which have occurred during exposure. It is because these mental changes are not appreciated in the earlier stages by the subject himself that anoxia is dangerous.

These symptoms may develop at any height between 15,000 and 25,000 ft., and their onset and severity are determined by three factors. First, the partial pressure of oxygen in the lungs; secondly, the duration of the exposure; and finally, the amount of muscular work performed. Very long flights at altitudes in the region of 10,000 ft. will produce similar effects if hard work is done or if the cold is severe. Above 25,000 ft. a failure in oxygen supply is followed by unconsciousness in a matter of minutes, and as a rule there is insufficient time for the intermediate symptoms to develop.

(*b*) *Night Vision.*—The rod cells in the retina are extremely susceptible to oxygen lack, and since they are responsible for vision at night one of the first signs of anoxia is impairment of this faculty. At 6,000 ft. in starlight conditions the range of vision is reduced by 10 per cent. if additional oxygen is not supplied. It is the practice of aircrew who require to preserve their night vision to take oxygen from ground level upwards.

(*c*) *Cold.*—Anoxia intensifies the effects of cold upon the body and therefore enhances the early onset of frost-bite and fatigue. An airman suffering from oxygen lack is more liable to frost-bite because the effect of anoxia on the cortex results in less care being taken to protect the body from cold. Also, exposure to cold causes vasospasm of the affected part and the consequent reduction in blood flow gives rise to tissue anoxia; this is aggravated if the circulating blood is not fully oxygenated. The rise in metabolism, due to cold, increases oxygen consumption, and it is therefore necessary to supply higher oxygen flows to those flying in cold conditions.

(*d*) *Fatigue.*—Oxygen lack causes the early onset of fatigue at relatively low altitudes, and its cumulative effect is particularly noticeable on long flights between 8,000 and 10,000 ft. Fatigue and headache are the most common sequelæ of prolonged oxygen lack, and these may persist for twenty-four hours after the normal oxygen tension has been restored.

(*e*) *Airsickness.*—Anoxia aggravates any tendency to airsickness.

The effects of anoxia at varying altitudes are summarised below :—

Altitude.	Effects.
Breathing Air :	
Any altitude above 5,000 ft.	Increased tendency to airsickness, fatigue, and frost-bite.
5 to 10,000 ft.	Impaired night vision. Fatigue.
10 to 15,000 ft.	Fatigue. Simple errors of calculation and manipulation.
15 to 25,000 ft.	Euphoria, irresponsibility, and aggression, or lethargy, drowsiness, and stupor.
25,000 ft. and above	Twitching of limbs, unconsciousness, and death, which occurs in about thirty minutes above 30,000 ft.
Breathing Oxygen :	
36,000 ft. upwards	Gradual decrease in blood saturation.
44,000 ft.	Maximum altitude permissible without pressure mechanism. The effects are similar to those at 19,000 ft. when breathing air.
At ground level after exposure	Psychological and physiological fatigue, headache ; up to twenty-four hours after exposure.

In the Royal Air Force it is the practice to use oxygen on all flights exceeding an altitude of 10,000 ft., and to use it from the ground upwards at night to preserve night vision.

(*f*) *Mountain Sickness.*—People who climb or travel to heights above 10,000 ft. are liable to suffer from mountain sickness if they remain at altitude for more than a few hours. The most prominent features are headache, nausea, vomiting, and breathlessness, all of which are much increased by exertion. These symptoms are relieved by acclimatisation.

(4) **Acclimatisation.**—Continuous exposure over a period of weeks to decreased atmospheric pressure will, after a time, enable the subject to live and work at altitudes. This accounts for the survival of natives in the Andes and Himalayas at heights well above 15,000 ft., and is due to the process of acclimatisation, which is the result of the following factors. First, a rise in the red cell count and a corresponding increase in the oxygen combining capacity of the blood. Secondly, the progressively increasing ventilation rate ; alkalosis following this is compensated by the kidneys excreting an alkaline urine. The acclimatised man can therefore breathe rapidly and yet maintain an approximately normal *p*H of the blood. Thirdly, changes occur in the tissue-oxidase systems which enable cells to function normally in spite of the reduced oxygen pressure of the blood. In spite of these factors some degree of increased breathlessness on exertion remains, due to the diminished alkali reserve of the blood.

It is interesting to note that after acclimatisation two members of the Mount Everest expedition reached a height of just over 28,000 ft. without using oxygen. If an unacclimatised airman had made a parachute descent on to the mountain at this height he would have become unconscious almost immediately, and would probably have died within one or two hours. Aircrew never remain long enough at altitude without oxygen for the signs of acclimatisation to become evident.

II. Expansion of Gas

(1) **Ears and Sinuses.**—The middle ear contains air at atmospheric pressure and is ventilated through the Eustachian tube. This occurs during swallowing when the muscles attached to the tube contract and open its pharyngeal ostium.

On ascent the air in the middle ear expands and passes down the Eustachian tube into the throat, thus equalising the pressure. During descent the pressure in the middle ear is decreased, and, to equalise this, air must enter it from the nasopharynx. Owing to the anatomy of the Eustachian tube this can only take place if the pharyngeal ostium is opened voluntarily as in swallowing, and this normally occurs about once a minute. While descending it may be necessary to ventilate the tubes by voluntary swallowing, or if the rate increases rapidly, to perform the Valsalva manœuvre. This is done by closing the mouth, holding the nose, and blowing with the cheeks pressed firmly against the teeth while the breath is held. Upper respiratory infections provide the commonest cause of failure to ventilate the middle ear on descent ; this gives rise to pain and deafness, and examination will show that the tympanic membrane is indrawn, and effusion and hæmorrhage may take place into the middle ear if the pressure is not equalised. Very rapid descent, where ventilation of the middle ear has not been possible, may cause rupture of the drum. It is obvious that if the ears cannot be ventilated on the ground by the Valsalva manœuvre, the subject should not be allowed to fly.

Similarly, pressure differences between the sinuses and the outside air will cause congestion and inflammation of the lining mucosa ; this will be accompanied by the typical pain of sinusitis. The frontal sinuses are those most commonly affected. Rapid descent will, therefore, aggravate sinusitis, and its presence should be a bar to flying.

(2) **Alimentary Canal.**—The volume of gas in the gastrointestinal tract expands with altitude, and at 25,000 ft. it is three times as great as at ground level, and over seven times at 40,000 ft. If the gas is not passed as flatus as it expands, it may become trapped in the loops of intestine, and the ensuing distension will provoke abdominal colic. In rare cases the distension may limit respiratory excursion, and cyanosis and collapse will follow. The discomfort due to abdominal distension varies with the rate of ascent ; it is rarely observed below 20,000 ft., and is less likely to occur if the rate of ascent is limited to 500 ft. per minute. Various articles of diet, such as peas and beans, aggravate the condition, and it is evident that foods which produce gas should be avoided before high flying. There is no doubt that liability to abdominal distension and colic are markedly increased by constipation.

III. Decompression Sickness and Compressed Air Illness

Decompression sickness is a disorder caused by a decrease in barometric pressure *per se*, and is associated with the presence of bubbles in the body fluids. These bubbles are mainly composed of nitrogen and occur because the amount of gas soluble in a given volume of fluid is directly proportional to pressure. At ground level the body fluids are saturated with nitrogen at the same partial pressure as that exerted by this gas in the atmosphere ;

however, on ascent the atmospheric pressure decreases and, since the amount of gas held in solution in the body fluids is diminished, bubbles are formed. Rapid ascent by airmen from ground level to altitudes above 30,000 ft. may result in decompression sickness, and it is considered that the symptoms experienced are probably the result of vasospasm caused by gas emboli.

The ætiology of decompression sickness is analogous to that of Compressed Air Illness or Caisson Disease, and the symptoms, though not identical, are similar. In compressed air illness the subjects are exposed to pressures greater than atmospheric, and then decompression to ground-level pressure is made quickly so that gas bubbles form in the body fluids. While the symptoms of decompression sickness are relieved by immediate descent to ground level, those of compressed air illness are treated by recompression and then returning to ground-level pressure more slowly.

Individual susceptibility to decompression sickness varies greatly, and it has been found that a large proportion of young, healthy adult males can remain at an altitude of 35,000 ft. without becoming affected. The incidence of symptoms is markedly increased by a rapid rate of ascent, since there is then less time for bubbles to be discharged into the alveolar air as the blood passes through the lungs. Temperature, time of day, and the amount of muscular exercise taken beforehand all influence susceptibility. The age and obesity of the subject are also important, since liability to the disorder increases with age and weight. The latter factor is probably the result of nitrogen being more soluble in fat at body temperature than in other tissues.

The earliest and most common symptom of decompression sickness and compressed air illness is an itching of the skin, which may be transient. It is frequently followed by pain in the region of the joints of the limbs, which is sufficiently severe to make the subject bend the limb to try and relieve the pain ; hence the name " bends." Retrosternal pain and coughing on inspiration may occur and are known as " chokes."

In a few instances fainting is observed, but this is rarely seen without warning and is accompanied by pallor, sweating, and an irregular pulse. In these subjects headaches resembling migraine occasionally persist after ground level has been reached, and defects in the visual fields may be noted. Very rarely this circulatory collapse has been followed by death after periods varying up to seventy-two hours. The clinical picture is one of shock, and a fall in blood pressure is always present. This is followed by gross pulmonary œdema and hydrothorax of doubtful origin.

In compressed air illness the signs and symptoms are more prolonged and severe. The lower dorsal segments of the spinal cord are frequently affected, and a permanent paraplegia may ensue. Cases of sudden death have been recorded from massive air embolism in the heart as a result of large quantities of nitrogen being liberated into the blood stream.

In theory, decompression sickness can be prevented if the rate of ascent is sufficiently slow to allow the excess gas to be given off in the alveoli as the blood circulates through the lung capillaries ; however, the rate of ascent necessary for this is too slow to make it practicable. Protection from decompression sickness is also possible if pure oxygen is breathed for several hours at ground level before ascent, thus replacing the nitrogen in the tissues and blood stream with oxygen. The most effective prophylaxis

is to enclose the individual in a pressure cabin, so that he is independent of the external atmospheric pressure.

Finally, a certain proportion of young and healthy individuals appear to be relatively insusceptible to the disease. In the Royal Air Force flying personnel are selected for very high altitude flights by subjecting them to a series of tests in a decompression chamber at an altitude of 35,000 ft., and rejecting those who develop incapacitating symptoms.

EFFECTS OF CHANGES IN ACCELERATION

Speed in itself does not produce any physiological effect on man if protection is given from high wind pressures by enclosing him in a cockpit. However, if motion changes either in direction or magnitude, the body undergoes great mechanical stress. It is customary to term an acceleration which forces the blood from head to feet as positive, and one which acts in an opposite direction as negative.

Centrifugal accelerations are the result of changes of the direction of motion and are commonly observed when an aircraft makes a tight turn. This acceleration is associated with an increase of apparent weight in both the aircraft and pilot, because weight is the product of mass and acceleration; on the ground, at rest, man is subjected to an acceleration towards the centre of the earth caused by the pull of gravity. This acceleration has the value of 32·2 ft. per sec. per sec. and is represented by the symbol g. To compare the magnitudes of centrifugal acceleration to which pilots are exposed in tight turns, the force is measured in units or multiples of g. Thus a centrifugal acceleration of 96·6 ft. per sec. per sec. is known as $3g$, and indicates a threefold increase in apparent weight.

The effects of centrifugal acceleration are caused by an increase in the weight of the body tissues and the blood, and depend upon the magnitude and duration of the force. The most important effect of centrifugal acceleration on the pilot is "black-out."

"Black-out," or the impairment of vision during active manœuvre in flight, was first observed clinically in this country when pilots of the Royal Air Force were practising for the Schneider Cup races in 1927. Blurring of vision and blindness were experienced in steep turns. "Black-out" is the result of centrifugal force applied to the long axis of the body. The increased weight of the blood prevents the heart from maintaining the hydrostatic column between heart and head, and encourages pooling in the abdomen and lower limbs. The consequent fall of blood pressure produces retinal ischæmia and "black-out." Continued application of centrifugal force leads to unconsciousness. "Black-out," however, precedes loss of consciousness because the intra-ocular pressure causes the retinal vessels to collapse while blood still flows through the brain.

The subjective sensations are those of a great increase in weight of all parts of the body, and the pilot feels forced into his seat. The apparent increase in weight causes the soft tissues of the face to sag.

Since it is impossible to alter the increased weight of the blood, measures to overcome "black-out" aim at decreasing the height of the hydrostatic column between heart and head, and at preventing blood from draining into the legs. In theory these objects could be obtained by assuming the

prone position, but this is not normally practicable in flight. However, " black-out " threshold may be increased by crouching forward and raising the legs as the centrifugal force is applied. Cockpit design can do much to make this easy, and during the battle of Britain pilots of the Royal Air Force obtained much benefit from crouching, tensing the abdominal muscles, and raising their feet on specially designed rudder pedals. Suits also have been developed consisting of trousers of inextensible material which extend up to the level of the heart. Within these trousers are a series of carefully placed bladders. In one type the bladders are filled with water and this exerts an equal and opposite pressure on the vessels in the lower limbs when centrifugal force is applied. If an air suit is worn, air is automatically pumped into the bladders when the centrifugal force has reached a certain level. It is essential that such suits should be sufficiently comfortable to be tolerated both in the air and on the ground when living in operational conditions.

Negative accelerations are rarely experienced, but will occur if an outside loop is made inadvertently. In these circumstances the pilot's head is away from the centre of the circle and blood is forced towards the vertex. A negative acceleration of about 3*g* gives rise to " redding-out " of vision. Higher values of negative *g* will cause conjunctival and petechial hæmorrhages above the heart level. Cerebral damage from rupture of vessels may occur, while loss of memory and headache following this manœuvre have been noted.

AIRSICKNESS

Airsickness is a form of motion sickness and is due to stimulation of the otoliths in the labyrinth of the inner ear by vertical, angular, and centrifugal accelerations. This produces reflex nausea and vomiting preceded by sweating and pallor. Change in vertical acceleration is the most important factor, and the incidence of airsickness can be correlated to the magnitude of this force.

Airsickness occurs most commonly in those who have a history of susceptibility to other types of motion sickness. This, however, was not apparent during the war when such an admission tended to disqualify a volunteer from flying training. Airsickness occurs in approximately 10 per cent. of all aircrew during the first twelve hours in the air. In the vast majority of cases adaptation to the accelerations of flight takes place, and airsickness only recurs in exceptional circumstances; however, a very small proportion are almost invariably airsick except in the smoothest weather. Adaptation may be broken by prolonged severe aerobatics, organic disease, the elapse of several months between flights, and on very long flights in extremely bumpy weather.

Prevention and alleviation of airsickness in prospective passengers is an important problem. Much can be done to reduce the incidence of airsickness by paying attention to the accessory factors which aggravate this condition. The magnitude of the vertical acceleration can be reduced by aircraft design and by planning the flight to avoid bumpy weather. Regulation of the heating system is important in order to maintain an even temperature. An adequate system of ventilation is of value in removing aircraft smells and the odour of vomitus. Particular attention should be

paid to diet, and light appetising meals or snacks served at frequent intervals are to be recommended. At night the aircraft should be adequately lit so that attention can be occupied by reading or other forms of relaxation. For flying by day, large windows giving an unobstructed view serve the same purpose. When possible, susceptible subjects should lie down.

Although a great variety of drugs have been used in the treatment of airsickness, two facts have emerged. First, a significant decrease in the incidence of airsickness is obtained by giving a placebo with reassuring advice. Secondly, of the various drugs investigated, hyoscine hydrobromide ($\frac{1}{120}$ gr.) is the most effective. Slightly better results are obtained with a compound tablet, the composition of which is as follows: hyoscine hydrobromide $\frac{1}{400}$ gr., benzedrine sulphate 2 mg., and sodium phenobarbitone $\frac{1}{8}$ gr. It is recommended that four tablets are taken half an hour before flying, and if signs of airsickness develop, two further tablets should be taken after two hours in the air.

Seasickness, like train and airsickness, is also a common form of motion sickness. Predisposition to one form of the disorder does not necessarily involve susceptibility to another. All forms of motion sickness are rare in infants and the aged, but those who suffer from migraine and cyclical vomiting are specially susceptible.

The symptoms of seasickness are essentially similar to those of airsickness, and the general principles of treatment are common to both. Larger doses of sedatives, however, such as phenobarbitone (up to 1 gr. four-hourly) or chloretone (5 gr. in cachets), are permissible in seasickness. In airsickness it is undesirable for the patient to become so drowsy that he cannot ventilate his middle ears either by swallowing or by performing a Valsalva manœuvre (*vide* p. 852).

ROLAND WINFIELD.

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NAMES MADE OFFICIAL BY MEANS OF ADDENDA TO THE BRITISH PHARMACOPŒIA, 1932, AND BY MEANS OF THE BRITISH PHARMACOPŒIA, 1948

PHARMACOPŒIAL NAMES	OTHER NAMES
Acetarsol	Stovarsol
Amphetamine	Benzedrine
Bromethol	Avertin
Carbachol	Doryl
Chiniofon	Yatren
Deoxycortone Acetate	D O C A
Diodone, Injection of	Perabrodil
Diphenan	Butolan
Dithranol	Cignolin
Ergotamine Tartrate	Femergin
Hexobarbitone	Evipan
Iodised Oil	Lipiodol
Iodoxyl	Uroselectan-B
Leptazol	Cardiazol
Menaphthone	Kapilon
Mepacrine Hydrochloride	Atebrin ; Quinacrine Hydrochloride, U.S.P. XIII
Mersalyl, Injection of	Salyrgan
Methylphenobarbitone (Phemitone)	Prominal
Neostigmine Bromide	Prostigmin
Nikethamide	Coramine
Oxytocin, Injection of	Pitocin
Pamaquin	Plasmoquine
Pentobarbitone Sodium	Nembutal
Pethidine Hydrochloride	Dolantin ; Demerol
Phenytoin Sodium	Epanutin
Sodium Aurothiomalate	Myocrisin
Stibophen	Fouadin
Sulphacetamide	Albucid
Theophylline with Ethylenediamine	Euphyllin ; Cardophylin
Thiopentone Sodium	Pentothal Sodium
Vasopressin, Injection of	Pitressin

TABLES OF APPROXIMATE EQUIVALENTS OF DOSES, APOTHECARIES' AND METRIC SYSTEMS

WEIGHTS

Apothecary or Troy.		Metric.
1 oz.	=	30 gm.
4 dr.	=	15 gm.
2½ dr.	=	10 gm.
2 dr.	=	8 gm.
75 gr.	=	5 gm.
1 dr.	=	4 gm.
45 gr.	=	3 gm.
30 gr.	=	2 gm.
15 gr.	=	1 gm.
10 gr.	=	0·65 gm.
7½ gr.	=	0·5 gm.
7 gr.	=	0·45 gm.
6 gr.	=	0·4 gm.
5 gr.	=	0·32 gm.
4 gr.	=	0·25 gm.
3 gr.	=	0·2 gm.
2½ gr.	=	0·16 gm.
2 gr.	=	0·13 gm.
1½ gr.	=	0·1 gm.
1 gr.	=	65 mg.
¾ gr.	=	50 mg.

Apothecary or Troy.		Metric.
⅔ gr.	=	45 mg.
½ gr.	=	32 mg.
⅜ gr.	=	24 mg.
⅓ gr.	=	22 mg.
¼ gr.	=	16 mg.
⅕ gr.	=	13 mg.
⅙ gr.	=	11 mg.
⅛ gr.	=	8 mg.
$\frac{1}{10}$ gr.	=	6·5 mg.
$\frac{1}{12}$ gr.	=	5·4 mg.
$\frac{1}{16}$ gr.	=	4 mg.
$\frac{1}{20}$ gr.	=	3·2 mg.
$\frac{1}{32}$ gr.	=	2 mg.
$\frac{1}{64}$ gr.	=	1 mg.
$\frac{1}{100}$ gr.	=	0·65 mg.
$\frac{1}{120}$ gr.	=	0·54 mg.
$\frac{1}{160}$ gr.	=	0·4 mg.
$\frac{1}{200}$ gr.	=	0·32 mg.
$\frac{1}{250}$ gr.	=	0·26 mg.
$\frac{1}{320}$ gr.	=	0·2 mg.
$\frac{1}{640}$ gr.	=	0·1 mg.

LIQUID MEASURES

Apothecary.		Metric.
1 pint (20 fluid oz.)	=	568 c.c.
12 fluid oz.	=	340 c.c.
8 fluid oz.	=	227 c.c.
6 fluid oz.	=	170 c.c.
4 fluid oz.	=	114 c.c.
3 fluid oz.	=	85 c.c.
2 fluid oz.	=	57 c.c.
1 fluid oz.	=	28·4 c.c.
4 fluid dr.	=	14 c.c.
2 fluid dr.	=	7 c.c.
1 fluid dr.	=	3·5 c.c.

Apothecary.		Metric.
50 min.	=	3 c.c.
45 min.	=	2·7 c.c.
30 min.	=	1·8 c.c.
20 min.	=	1·2 c.c.
15 min.	=	0·9 c.c.
10 min.	=	0·6 c.c.
8 min.	=	0·5 c.c.
5 min.	=	0·3 c.c.
3 min.	=	0·18 c.c.
2 min.	=	0·12 c.c.
1 min.	=	0·06 c.c.